Case-control study of risk factors for Legionnaires' disease caused by *Legionella longbeachae* in Canterbury, New Zealand

by

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Abstract

Introduction

Legionnaires' disease is a form of atypical pneumonia caused by infection from *Legionella* bacteria. There is a known association between the use of compost-based soil products and Legionnaires' disease caused by the bacterium *Legionella longbeachae*. A case-control study was carried out between October 2013 and March 2014 in Canterbury, New Zealand, where reported prevalence of *L. longbeachae* infection is unusually high, to investigate host risk factors and gardening-related risk factors for the disease.

Methods

Twenty-one laboratory-confirmed notified cases and 69 population controls were interviewed using a structured questionnaire. Logistic regression was used in STATA 13 to calculate univariate odds ratios for variables of interest. Stratified univariate analysis was undertaken to consider the impact of multiple risk factors on disease risk.

Results

Having smoked for 10 or more years (OR 4.00, 95% CI 1.42-11.24) was strongly associated with *L. longbeachae* infection. Having an indoor garden also increased disease risk (OR 3.81, 1.18-12.27). Use of compost-based products during the three-week reference period (OR 4.16, 1.37-12.64) was associated with *L. longbeachae* infection. Opening (OR 4.6, 1.64-12.92) and tipping or troweling potting mix or purchased compost (OR 5.00, 1.71-14.5), and touching the face after using these

products before washing hands (OR 12.22, 3.16-47.29) were also strongly associated with disease. Having hanging pots or baskets (OR 0.77, 0.27-2.17) and being near dripping hanging pots or baskets (OR 0.38, 0.27-2.17) during the three-week reference period were not associated with disease, as had been observed in a previous case-control study conducted in South Australia from 1996-98. Wearing a mask (OR 1.80, 0.30-10.64) or gloves (OR 0.64, 0.15-2.77) while using potting mix did not appear to be protective against disease.

Discussion

Long-term smoking is an important risk factor for *L. longbeachae* Legionnaires' disease, and those with a history of smoking for more than 10 years should be advised to exercise extreme caution when using compost-based products. Important environmental risk factors include use of potting mix or purchased compost, poor hand hygiene while using compost-based products, and other behaviour that transfers these products to the mouth or face. Use of compost-based products indoors may also increase risk. The findings suggest that transmission of bacteria from the environment to humans may occur through aspiration of contaminated soil particles that are transferred to the mouth. Hand-washing and keeping potting mix and compost away from the face appear to be key measures for preventing Legionnaires' disease.

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1 Introduction

1.1 Thesis overview

This thesis describes a case-control study of Legionnaires' disease, a form of pneumonia, caused by the bacterium *Legionella longbeachae.* The study was carried out during the period from October 2013 to March 2014 in the Canterbury region of New Zealand.

Legionnaires' disease is the most commonly identified cause of pneumonia in Canterbury during the spring and summer seasons (D. Murdoch, personal communication). It causes severe disease, occurs in a predictable seasonal peak, and is potentially preventable. Only one case-control study of *L. longbeachae* infection has been undertaken previously, in South Australia in 1997-1999 (1).

L. longbeachae inhabits soil media containing decomposed plant matter, such as potting mix and compost (2), and gardeners who handle these products are known to be at risk of contracting the disease (1). The study considers this and other possible gardening-related risk factors for *L. longbeachae* Legionnaires' disease in order to inform disease prevention measures and future research. The findings may contribute to the development of a more robust body of evidence upon which to base health promotion messages about gardening-related risk factors and measures for preventing disease.

1.1.1 Local context

Canterbury has a relatively high incidence of Legionnaires' disease compared to other regions of New Zealand and the world, with most reported cases being caused by infection from *L. longbeachae* bacteria, as opposed to other species of Legionella, such as

Legionella pneumophila (3). Legionnaires' disease accounts for approximately 20% of community-acquired hospitalised pneumonia cases in Canterbury during the spring and summer seasons, making it the most commonly identified cause of pneumonia over this period (D. Murdoch, personal communication). Christchurch has the reputation of being New Zealand's "Garden City," and public and media interest in Legionnaires' disease has grown in recent years due to the increasing number of hospitalisations and deaths attributed to *Legionella* bacteria associated with potting mix and gardening.

The introduction of routine Polymerase Chain Reaction (PCR) testing of all hospitalised pneumonia cases in Canterbury in 2010 revealed that the burden of Legionnaires' disease was much higher than was previously realized. 114 cases of Legionnaires' disease were laboratory-diagnosed in Canterbury between 2008 and 2012; 30% of cases were admitted to the intensive care unit and 11% died (4). Approximately two thirds of notified cases in Canterbury had used compost or potting mix products in the weeks prior to illness (P. Mitchell, personal communication). Despite considerable efforts to promote safe handling of potting mix beginning in 2012, preventive measures did not lead to a reduction in cases leading up to the 2013-2014 Legionella season.

Use of compost-based products alone is not a sufficient explanation for the disease, as many people in Canterbury use these products during spring and summer and very few become ill. It is likely to be some combination of personal characteristics, such as smoking, pre-existing respiratory disease or immunosuppression, and the way in which people use potting mix and compost that determines who contracts the disease.

1.1.2 Aim and objectives

The aim of the study was to improve our understanding of risk factors, beyond just use of compost-based products, for Legionnaires' disease caused by *L. longbeachae* in Canterbury.

The objectives of the study were as follows:

1. Investigate host risk factors for Legionnaires' disease caused by *L. longbeachae*, including demographic characteristics, health status, and smoking history
2. Investigate environmental, gardening-related risk factors for *L. longbeachae* Legionnaires' disease and possible modes of transmission of *L. longbeachae* bacteria from environmental sources to humans
3. Evaluate the effectiveness of existing measures to prevent Legionnaires' disease, such as wearing gloves and a mask when handling potentially contaminated materials
4. Formulate recommendations based on the findings relating to health promotion messaging for disease prevention and future epidemiological research into *L. longbeachae* Legionnaires' disease in Canterbury and further afield

The Canterbury study might also serve as a pilot study for a larger national case-control study of Legionnaires' disease in New Zealand. Ultimately, it is hoped that the growing body of epidemiological research into *L. longbeachae* Legionellosis will assist with the development of more effective interventions to prevent Legionnaires' disease, and to reduce pneumonia hospitalisations and death.

1.1.3 Role in the study

I was a student investigator and study coordinator for the study. My role involved overseeing the planning and implementation of the study between July 2013 and April

2014 under the guidance of my supervisors, Associate Professor Patricia Priest (Department of Preventive and Social Medicine, University of Otago) and Professor David Murdoch (Department of Pathology, University of Otago, Christchurch School of Medicine), with the support of an advisory group from Community and Public Health, the Canterbury District Health Board's public health unit, made up of Debbie Smith, Dr Peter Mitchell, Dr Alistair Humphrey, and Dr Ramon Pink.

The scope of my involvement encompassed obtaining ethics approval and locality authorisation for the study; undertaking consultation with Māori; reviewing the literature and available information on Legionnaires' disease and *L. longbeachae* infection; developing the study questionnaire; developing standard operating procedures for the implementation of the study and data collection; recruiting controls and undertaking a approximately half of the control interviews; providing oversight for case data collection; and performing data entry. I also planned and independently undertook the analysis of the data with guidance from my supervisors and Dr Claire Cameron, a biostatistician in the Department of Preventive and Social Medicine, University of Otago.

1.2 Background

The following search strategy was used to gather background information on *Legionella* bacteria and Legionellosis, and to undertake a review of published research on *L. longbeachae* Legionnaires' disease. Ovid Medline 1946-present database was used to search keyword and subject heading terms:

exp Legionella longbeachae/

exp Legionnaires' disease/ exp New Zealand

Legionnaires' disease/ AND Community-acquired infections/ AND Risk factors

Legionnaires' disease/mi [Microbiology] limit to "review articles"

Legionella/mi [Microbiology] limit to "review articles"

Legionnaires' disease/di [Diagnosis] limit to "review articles"

Legionnaires' disease/hi [History]

Legionellosis/ep [Epidemiology]

Legionellosis/pc [Prevention & Control]

Published research on *L. longbeachae* is limited; the term 'Legionella longbeachae' returned only 32 results and all relevant articles were reviewed. Only one case-control study of risk factors for *L. longbeachae* infection was found in the peer-reviewed literature (1). The term 'Legionnaires' disease' yielded several thousand results and subheadings were used to produce more specific searches. International surveillance reports were sourced from relevant agency websites for countries and regions that routinely monitor Legionellosis cases.

This section presents general background and historical information on Legionnaires' disease, a brief overview of *Legionella* bacteria and the pathogenesis of Legionnaires' disease in humans, and a summary of clinical features and diagnosis. Section 1.3 provides an overview of the epidemiology of Legionnaires' disease and *L. longbeachae* infection in New Zealand and internationally. Due to the dearth of published research relating specifically to *L. longbeachae*, a formal literature review is not presented, however Section 1.4 presents the results of the case-control study of *L. longbeachae* conducted in South Australia in 1997-1999 and provides a critical appraisal of the study design. The remainder of that section summarises host and environmental risk factors for

Legionnaires' disease, with a focus on *L. longbeachae* infection, and discusses possible modes of transmission of *Legionella* bacteria from environmental sources to humans.

1.2.1 *Legionella* and Legionnaires' disease

Legionnaires' disease is a form of respiratory disease in humans caused by infection from *Legionella* bacteria. The disease was first identified after an outbreak of severe pneumonia during an American Legion Convention in Philadelphia in August 1976 (5). The outbreak was traced to the lobby of one convention hotel, and epidemiological investigation concluded that the mode of spread was most likely airborne, although the etiologic agent was not identified (5). Several months later, a gram-negative bacterium was cultured from lung tissue samples of four deceased patients and confirmed as the etiologic agent of the disease through antibody testing of serum specimens from disease survivors, as well as stored specimens from two previous outbreaks of respiratory disease (6). The *Legionella* genus was later established in 1979 and the species responsible for the Philadelphia outbreak was identified as *Legionella pneumophila* (7).

Fifty-eight species of *Legionella* have been classified in recent decades and 30 of these have been found to be associated with disease in humans (8). Like *L. pneumophila*, most Legionellae are aquatic bacteria inhabiting freshwater environments as parasites of protozoa (9), surviving and multiplying at temperatures between 20°C and 50°C (10). Sporadic occurrence and outbreaks of Legionnaires' disease are usually attributed to man-made environments, such as swimming pools, hot water systems, and cooling towers. *Legionella* are transmitted to humans through inhalation or aspiration of contaminated water particles. The pathogens replicate in the alveoli of the lungs of susceptible hosts, causing inflammation and tissue damage, which leads to systemic infection (9). The

incubation period of *Legionella* infection is thought to be 2-14 days (10), although one study reported an incubation period of up to 19 days (11). Some species of Legionella, including *Legionella longbeachae,* more frequently inhabit soil than water, and their transmission to humans is not fully understood (8) (12).

1.2.2 Clinical features and diagnosis

Legionnaires' disease is characterized as an acute atypical pneumonia with respiratory, gastrointestinal, and neurological symptoms (10, 13). A second clinical presentation of infection from *Legionella* bacteria is a less severe flu-like illness known as Pontiac Fever. It remains unclear if Legionellosis presents only in these two discrete forms, or on a clinical spectrum from asymptomatic to severe disease (7). The clinical symptoms of *L. longbeachae* infection were initially observed to be indistinguishable from those of pneumonia caused by other *Legionella* species (14). This was validated by a 2009 retrospective review of 50 culture-positive cases of Legionnaires' disease in Canterbury, which found no significant difference between cases caused by *L. longbeachae* and *L. pneumophila* in terms of prevalence of predisposing factors, clinical features, and disease severity and outcomes (8). Importantly, Legionnaires' disease is also clinically and radiographically indistinguishable from other causes of pneumonia, making detection and appropriate treatment more challenging (4, 13). *Legionella* is not susceptible to β-lactam antibiotics used to treat typical community-acquired pneumonias, which reinforces the need for effective diagnostic approaches to provide effective treatment (15). Routine laboratory testing of hospitalised pneumonia patients for Legionnaires' disease may be the most effective method of diagnoses, however this approach is uncommon outside of Canterbury (4, 16).

Legionnaires' disease is a notifiable condition in New Zealand and many other countries due to the potential for outbreaks of infection caused by *L. pneumophila* and some other legionella species (17, 18). Despite this, it is likely that the disease is significantly under-diagnosed throughout the world due to its similarity to other types of pneumonia, a general lack of awareness of clinical and public health implications of the disease, and absence of routine testing strategies in many countries. Widely-used urinary antigen tests for *Legionella* are often specific to *L. pneumophila,* resulting in the over-representation of this species in disease surveillance data and under-detection of infection caused by other species (7). Options for diagnostic testing have increased dramatically in recent years and now include urinary antigen detection for several species, sputum culture, serological testing, and more recently, polymerase chain reaction (PCR) testing of clinical samples (16, 19).

1.2.3 Legionella longbeachae

Legionella longbeachae was first isolated from human lung tissue samples in 1980 following four cases of Legionnaires' disease caused by *L. longbeachae* in the United States (14). Although the environmental source of the bacteria was not determined for several years, the species was named after Long Beach, California, the location where the first infected patient was hospitalised.

Unlike *L. pneumophila*, *L. longbeachae* rarely inhabits aquatic environments and instead thrives in soil, particularly in decomposing plant matter (20). An association between *L. longbeachae* and gardening soil products, such as compost and potting mix, was established in 1989 following epidemiological investigation of an outbreak of 30 cases of *L. longbeachae* Legionnaires' disease in South Australia (2). Case interviews revealed

that gardening was a common activity for many cases and may be a risk factor for the disease. *L. longbeachae* was then isolated from samples of potting mix used for gardening by four of the confirmed cases, and subsequently from several samples of composting plant matter obtained from home gardeners and commercial facilities (21). *L. longbeachae* associated with gardening and compost-based products has since been identified as a causative agent of Legionnaires' disease in New Zealand, the United States (22), Western Europe (20, 23-25), and East Asia (26-28).

L. longbeachae and compost-based products

A 1990 study found that over 70% of 45 varieties of Australian potting soils tested positive for *L. longbeachae,* compared to none of 19 European potting mixes tested (2). *L. longbeachae* has also been cultured from potting mix in the United States following three cases of *L. longbeachae* Legionnaires' disease in the states of Washington, Oregon, and California on the West Coast (22). It has been hypothesised that *L. longbeachae* and other *Legionella* species thrive in wood-based compost products that are popular in New Zealand, Australia, the United States, and Japan (26), and not the mainly peat-based compost products found in Europe (2). More recent isolation of *L. longbeachae* in potting soil in Scotland (12), Greece (23), Switzerland (20), and the Netherlands (24), suggests that *Legionella* may have a greater prevalence in European potting soils than first reported.

The manufacture of compost-based products in Canterbury occurs as three separate processes: green (plant) waste composting; food waste and biosolids composting; and composting bark to make potting mix (G. Fietje, personal communication). The processes for green waste composting and bark composting for potting mix are very

similar. Green waste is shredded and piled in windrows, and turned weekly for 12 weeks, adding water as necessary to maintain adequate moisture. Bark is ground, screened, and composted in windrows with fertilisers and lime, and turned regularly for 6-12 weeks. After composting, both products are blended with additives, such as fertilisers, bark, pumice, and sand to make specialist mixes, which are sold in bulk and bagged (G. Fietje, personal communication).

1.3 Descriptive epidemiology

1.3.1 *L. longbeachae* in New Zealand and Canterbury

Legionellosis notification rates in New Zealand remained relatively stable between 1997 and 2009 (29), when the number of notified cases rose from 74 (a rate of 1.7 per 100,000 population) in 2009 to 173 (4.0 per 100,000 population) in 2010 as shown in Table 1 (30).

Table 1. Number and rate per 100,000 population of notified Legionellosis cases in Canterbury and all New Zealand, 2008-2012

	2008		2009		2010		2011		2012	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
Canterbury	12	2.4	14	2.8	62	12.2	65	12.9	52	10.4
New Zealand	73	1.7	74	1.7	173	4.0	158	3.6	152	3.4

In 2012, 152 cases of Legionellosis were notified in New Zealand, representing a rate of 3.4 per 100,000 population (3). 98 cases were male (64.5%) and nearly 60% of cases were over 60 years of age. There were 6 reported deaths due to Legionellosis in 2012, resulting in a case fatality ratio of 3.9% for notified cases. Environmental sources of infection were reported for 84 cases, and of these 52 cases reported exposure to compost, potting mix, or soil (3). As shown in Table 1, disease rates for Canterbury in 2012 were

substantially higher than the national rate with 52 cases notified at a rate of 10.4 per 100,000 population, with rates for other District Health Boards ranging from 2.2 to 4.2 per 100,000 (31).

The jump in case notifications in 2010 is at least partially attributable to changes in the testing strategy for Legionellosis in Canterbury. In November 2010, Canterbury Health Laboratories introduced routine PCR testing of respiratory specimens from all hospitalised pneumonia patients for a two-year period (4). Subsequently, 92 cases of Legionnaires' disease were identified from November 2010 to October 2012, compared to only 22 in the two-year period between November 2008 and October 2010 immediately before routine PCR testing was introduced. The findings indicate that the burden of Legionnaires' disease in Canterbury is much higher than was previously realized. Of the 114 cases identified during the four-year study period, 95 (85%) were *L. longbeachae* infection, and 14 (15%) were caused by *L. pneumophila*. The study also demonstrated that the severity of the disease is great. Between 2008 and 2012, 30% of Legionnaires' disease cases in Canterbury were admitted to the intensive care unit and 11% died (4).

Table 2. *Legionella* species for laboratory-reported cases, 2008-2012

	2008		2009		2010		2011		2012	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
L. longbeachae	38	51.4	32	41.6	72	40.4	70	43.8	78	51.3
L. pneumophila	25	33.8	34	44.2	51	28.7	48	30.0	51	33.6
Other *Legionella* species	11	14.9	13	16.9	55	30.9	42	26.3	23	15.1
Total	74		77		178		160		152	

Table 2 shows that *L. longbeachae* has been the most prevalent *Legionella* species since 2010. Of the 52 Canterbury cases reported in 2012, 40 (76.9%) were *L. longbeachae*

infection and most cases were reported during the period from October through March (31). Disease surveillance as shown that two thirds of all notified Legionellosis cases in Canterbury had been exposed to compost or potting mix (P. Mitchell, personal communication).

1.3.2 International surveillance

Internationally, most reported cases of Legionnaires' disease are caused by *L. pneumophila*, including 90% of reported cases in the Unites States (7) and 95% of reported cases in Europe (20). The incidence of *L. longbeachae* infection is not well described worldwide due to the absence of routine surveillance in many countries and limitations of diagnostic testing.

In Australia, however, *L. longbeachae* is recognised as the dominant causative agent of Legionnaires' disease (32), as it is in New Zealand. Legionellosis became a notifiable disease in Australia in 1991, and case numbers have continued to rise since then (32). 382 cases of Legionellosis were notified in Australia in 2012, representing a rate of 1.7 per 100,000 population (32). 61% of cases were male and rate of notification increased with age, being highest for males over 85 years at a rate of 10.7 per 100,000 population. There were 11 deaths due to Legionellosis reported, resulting in a case fatality ratio of 2.9%. 190 cases (49.7%) were *L. longbeachae* and 163 (42.7%) were *L. pneumophila.* South Australia had the highest notification rate of Legionellosis cases of all territories with 3.4 per 100,000 population, as well as the greatest proportion of *L. longbeachae* cases (73 of 85 cases) (32).

In the United States, the National Notifiable Disease Surveillance System coordinates the reporting of notifiable disease by state health departments (33). From 2000-2009, 22,418 cases of Legionellosis were reported and the crude incidence rate rose from 0.39 per 100,000 population to 1.15 per 100,000 population. Seventy-four percent of cases were over 50 years of age and 64% were male (33). *Legionella* species is not reported, however the diagnostic case definition for Legionellosis is "recovery of Legionella sp. in culture, detection of Legionella pneumophila serogroup 1 antigen in urine, or fourfold or greater rise in L. pneumophila serogroup 1-specific serum antibodies" (33), which means that routine testing would often not detect non-*L. pneumophila* cases. Three cases of *L. longbeachae* Legionnaires' disease were reported in May and June 2000 in the West Coast states of Washington, Oregon, and California (22). Two of the cases were investigated and *L. longbeachae* was isolated from potting soil samples used by both patients during the disease incubation period.

The European Centre for Disease Prevention and Control undertakes surveillance of Legionnaires' disease for 29 European countries. 5852 cases were notified in 2012, representing a rate of 1.15 per 100,000 population (34). Rates of notification ranged from 0.0 in Bulgaria to 3.99 per 100,000 population in Slovenia. The median age at date of onset was 61 years, and 79% of cases were over 50 years of age. Over 70% of notified cases were male (34). The case fatality ratio was 10% based on cases with a known outcome. European surveillance is largely *L. pneumophila* focused; 79% of laboratory tests performed were urinary antigen tests specific to *L. pneumophila,* meaning that cases of Legionnaires' disease caused by other *Legionella* species are likely to be overlooked. Of 649 culture-confirmed cases in 2012, one case of *L. longbeachae* was confirmed (34).

In recent years, Scotland has had the highest reported incidence of *L. longbeachae* cases of any country in the UK and Europe, leading to an increased interest in the genus by Health Protection Scotland (25). The first case of Legionnaires' disease caused by *L. longbeachae* in Scotland that was not associated with travel was notified in April 2008 (35). At the end of 2013, 18 cases had been reported over the six-year period, including a cluster of eight cases notified during August and September 2013 (36). All cases survived and there was a median age of 70 for the 2013 cases. Unlike the rest of the United Kingdom, the Scottish *Legionella* Reference Laboratory undertakes routine PCR and *L. longbeachae* specific serology testing of all possible cases of Legionnaires' disease, which may help to explain the increased number of *L. longbeachae* cases detected in Scotland (36).

Other countries in Europe have reported sporadic cases of *L. longbeachae* Legionellosis and identified compost-based products that tested positive for the species. One fatal case was reported in the Netherlands between 2004, and *L. longbeachae* was cultured from potting mix collected from the patient's home (24). Four further cases were then retrospectively identified from patient-derived *Legionella* isolates.

Legionnaires' disease is a notifiable disease in Taiwan, and the first case of *L. longbeachae* infection occurred in 2006. Six *L. longbeachae* cases were identified during 2006-2010, representing 1.2% of laboratory-confirmed cases of Legionnaires' disease (27). Two cases were male and four were female, and the median age was 73.5. One case died. Only two cases reported exposure to soil in the weeks prior to illness.

Active surveillance of severe clinical pneumonia in a rural region of Thailand in 2003-2004 revealed that the incidence of pneumonia caused by *L. longbeachae* was 5-29 cases per 100,000 of population (28). The rate of cases increased with age to 47 per 100,000

population for patients over 70 years of old. There was a male to female ratio of 1.6 for *L. longbeachae* cases. Agriculture is the primary industry in the region of Sa Kaeo where this study took place, and soil exposure is hypothesized to be a risk factor for disease.

1.4 Risk factors

1.4.1 South Australian *L. longbeachae* case-control study

Only one case-control study of risk factors for *L. longbeachae* infection was found in the peer reviewed published literature (1). The study was conducted in South Australia and included 25 cases reported between April 1997 and March 1999 and 75 controls matched for age, sex, and postcode. The study built on the findings of the earlier investigation of an outbreak of *L. longbeachae* infection in South Australia in the late 1980s, which linked the illness to gardening rather than the water sources typical of *L. pneumophila* infection (2) (37). All participants were interviewed over the telephone using a structured questionnaire that covered potting mix exposure, garden environment, and gardening behaviour and practices, as well as participant characteristics including health status and smoking history.

Descriptive and matched univariate analysis of all exposure variables and *L. longbeachae* revealed that exposure to potting mix was a risk factor for disease, as were health status, smoking history, some features of the garden environment, and hygiene practices related to gardening. Those who reported using potting mix in the last four weeks were nearly five times as likely to have developed disease (OR 4.74, 95% CI 1.65-13.55). Being near dripping hanging pots (OR 2.79, 1.05-7.47) was also identified as risk factor. Respondents with pre-existing cardiac illness (OR 7.29, 1.52-34.98) or respiratory illness

(OR 17.62, 2.15-144.25) were overrepresented in the case group and at increased risk of developing *L. longbeachae* infection. Having ever smoked (OR 5.79, 1.56-21.58) was associated with illness, as was having smoked for more than 30 years (OR 7.67, 1.86-31.58). Eating or drinking when gardening before washing hands (OR 6.22, 1.95-19.77) was also positively associated with illness. Although the odds ratios were higher for the health, smoking, and hygiene variables than for potting mix exposure alone, the wide confidence intervals indicate that the analysis was limited by the small sample size. This is particularly the case for the health variables, which were based on very few exposed cases.

In multivariate analysis, having smoked for more than 30 years (OR 19.16, 2.25-163.21) and not washing hands after gardening before eating or drinking (OR 29.47, 1.96-412.14) were the strongest predictors of illness. Being near dripping hanging pots (OR 8.97, 1.41-56.96) was also reinforced as an important risk factor. Again, the wide confidence intervals indicate the limitation of sample size on the strength of these findings. Interestingly, the authors state that exposure to potting mix was associated with disease in univariate analysis only (1), although this variable is not reported in the multivariate results to confirm this statement.

In addition to the small sample size, further limitations may have been introduced through the study design. Selection bias would have arisen due to controls being recruited from a database of respondents from another health survey. This group had previously agreed to participate in future studies and may have been more health conscious than the general population, which would bias the associations between risk factors and illness observed in the findings.

Overall, the findings of the study make an important contribution to existing knowledge of risk factors and possible modes of transmission of *L. longbeachae* infection determined through disease surveillance and descriptive epidemiological investigations in South Australia and internationally. The results demonstrate that intrinsic and behavioural factors may be as, or more, important to consider than environmental exposures alone.

1.4.2 Host risk factors

A number of notable case characteristics and possible gardening-related risk factors for *L. longbeachae* infection have been identified through disease surveillance processes, international case studies, case series reviews, and in the South Australian case-control study (1). These are summarized below in terms of intrinsic or host risk factors, environmental exposures, potential modes of transmission of *L. longbeachae* bacteria, and possible protective factors. Many of the demographic and health-related characteristics are risk factors for community-acquired pneumonia and Legionnaires' disease in general.

Case characteristics

Demographic risk factors for *L. longbeachae* infection resemble those of community-acquired pneumonia generally (38). Cases are usually middle-aged or older and more likely to be male than female. The median age of cases in the South Australian study was 71, and 18 of 25 cases (72%) were male (1). Similarly, the median age of *L. longbeachae* cases in Canterbury reported between 1998 and 2008 was 73.4 and 83% were male (8). For all detected cases of Legionellosis in Canterbury between 2008 and 2012 (85% of which were *L. longbeachae*), the median age was 65 and 68% were male (4). This was

similar to a mean age of 65 years for a series of six *L. longbeachae* cases in Scotland during 2008-2009 (25) and 67.7 years for a further seven cases reported during 2012-2013 (39).

Smoking

Current or former smoking is a common characteristic observed in cases, and is a known risk factor for community-acquired pneumonia (40). In a review of surveillance data for Legionellosis from all species of *Legionella* in New Zealand, 25% of cases from 1997 through 2009 were identified as being current or ex-smokers (41). In the South Australian study, 52% of cases had smoked for more than 30 years, compared to only 20% of controls. Having ever smoked and history of long-term smoking were also associated with illness (1).

Health status

Pre-existing illness is another common feature among cases. A review of 1997-2009 surveillance data for Legionellosis from all species of *Legionella* reported in New Zealand found that 38% of cases were identified as having pre-existing immunosuppression or otherwise debilitating condition, which was defined as including 'diabetes, chronic lung disease, cancer, transplant recipient and corti-costeroid treatment' (41). As discussed previously in section 1.4.1, the proportion of cases in the South Australian case-control study reporting cardiac, respiratory, and other medical conditions was greater than that of controls. Cases were also more likely than controls to have diabetes or immunosuppression.

1.4.3 Environmental risk factors, transmission, and prevention

Gardening and exposure to compost-based products

As discussed previously, *L. longbeachae* has been isolated from compost-based soil products in New Zealand and several other regions of the world and has been shown to be a causative agent of Legionnaires' disease. The South Australian case-control study and disease surveillance undertaken locally in Canterbury have demonstrated an association between the use of these products during gardening and disease. The process of disease transmission from environmental sources to humans is not fully understood and, consequently, it remains unclear how variation in the nature of exposure, individual behaviour, and use of precautionary measures may affect disease risk.

Exposure to contaminated water

The presence of ferneries or hanging pots at cases' homes was noticed in South Australia following a series of *L. longbeachae* cases in the late 1980s (37). It was hypothesized that transmission of soil-dwelling *L. longbeachae* to humans may occur through inhalation or aspiration of aerosolised contaminated water, similar to the transmission of aquatic *Legionella* species such as *L. pneumophila*, and that this process was aided by baskets hanging at head height. The hypothesis was supported by the results of the case-control study, which found that being near dripping hanging pots increased disease risk (1).

Inhalation or aspiration of contaminated particles

Hand-washing and hygiene practices related to gardening were also highlighted as important factors in the South Australian study. Eating or drinking when gardening before washing hands was positively associated with illness, and this was found to be a strong predictor of illness in multivariate analysis (1). This finding suggests that transmission of

L. longbeachae from compost-based products may occur through inhalation or aspiration of contaminated soil particles that are transferred directly to the face or mouth.

Disease prevention

Health promotion campaigns relating to safe use of potting mix and compost while gardening are implemented during spring and summer in Canterbury and throughout New Zealand. In "The Prevention of Legionellosis in New Zealand: Guidelines for the Control of Legionella Bacteria", the New Zealand Ministry of Health recommends several precautionary measures to reduce risk of *L. longbeachae* infection, "including the following:

- Wear a face mask when handling soil, mulches, compost or potting mix indoors or in windy conditions.
- Open the bag using a blade with care to avoid inhaling airborne potting mix, ie, slowly and away from the face.
- Moisten the contents of the bag on opening, by making a small opening and insert a garden hose to dampen the potting mix.
- Avoid potting-up plants in unventilated areas, such as enclosed greenhouses or sheds.
- Wear gloves.
- Avoid transferring potting mix from hand to mouth (eg, rubbing face with a soiled hand or glove).
- Always wash hands after handling potting mix, even if gloves have been worn, as *Legionella* bacteria can remain on hands contaminated by potting mix.
- Store potting mix in a cool place, away from the sun.
- Keep soils and potting mix damp.
- Avoid raising soil near evaporative coolers.
- Water gardens and composts gently, using a low-pressure hose.
- When handling bulk quantities of potting mixes or other soil products, follow procedures that minimise dust generation."(18)

Use of face masks and gloves was not reported as being protective against disease in the South Australian case-control study, although awareness of the risks associated with potting mix use was found to be a protective factor (1). Due to the limited amount of

research into Legionnaires' disease associated with compost-based products, the effectiveness of these measures in reducing disease risk is not known.

2 Methods

3.1 Study design

This study was designed to compare the features and recent exposures of identified cases of *L. longbeachae* infection in Canterbury to controls from the general population during the study period of 1 October 2013 to 31 March 2014. Trained interviewers used a structured questionnaire to collect information on individual characteristics and recent environmental exposures, including known and potential risk factors for *L. longbeachae* Legionnaires' disease, from cases and controls. Descriptive, univariate, and multivariable analysis was undertaken to identify or validate important risk factors for disease.

2.1.1 Justification for case-control study

A population-based case-control study was the most appropriate and efficient design for this research project. *L. longbeachae* Legionnaires' disease is a rare infection affecting a very small proportion of the population. Case-control studies make use of all identified cases within a defined population during a specified time period. There are a relatively large number of *L. longbeachae* cases diagnosed in Canterbury, and routine PCR testing of all hospitalised pneumonia patients for Legionella means that case identification already occurs and ascertainment level is likely to be high. Cases are also already routinely followed up by Health Protection Officers, which simplifies data collection by making use of existing resources within the public health unit to identify and gather information from cases. A sample of 40 cases and 120 controls will provide at least 80% power to detect odds ratios of 3 and above with a two-sided confidence level of 95% for exposure to compost, which occurs in two thirds of notified *L. longbeachae* cases (42).

2.1.2 Study organisation

The study was planned and carried out in conjunction with Community and Public Health, the public health unit of the Canterbury District Health Board. A steering group was formed in mid-2013 to assist with planning and operationalization of the study. Members of the steering group included faculty from the Department of Pathology and the Department of Preventive and Social Medicine at the University of Otago, me (the Study Coordinator), three Medical Officers and a Health Protection Officer employed by the Canterbury District Health Board. This group provided advice and assistance during the initial stages of study design and questionnaire development during July-September 2013.

Ethics approval to undertake the study was received from the University of Otago Human Ethics Committee (Health) in September 2013. Locality Authorisation for the Canterbury District Health Board was obtained and approved by the University of Otago, Christchurch.

Interviewers used a structured questionnaire to collect information on individual characteristics and recent environmental exposures, including known and potential risk factors for *L. longbeachae* Legionnaires' disease, from participants in both groups. Descriptive, univariate, and multivariable analyses were undertaken to compare data collected from cases and controls.

2.2 Participant recruitment

Legionnaires' disease is a notifiable disease in New Zealand and the study made use of the usual process for identifying and following-up notified cases. The procedure for case

selection was set out in the Standard Operating Procedure: Case Recruitment and Data Collection (Appendix A).

Surveillance data from past years was used to determine the expected number of *L. longbeachae* cases. It was estimated that up to 40 cases would be notified during the study period based on the notification of 40 *L. longbeachae* cases in Canterbury in 2012 (31). Three controls per case were included in the study, resulting in expected recruitment of 120 controls.

2.2.1 Case identification

For the purposes of the study, a case of Legionnaires' disease due to *Legionella longbeachae* was defined as a person notified to CPH who met the following three criteria:

- Any patient with a positive culture or PCR for *L. longbeachae* or who had a ≥4-fold increase in reciprocal *L. longbeachae* antibody titres; and
- Had an estimated disease onset between 1 October 2013 and 31 March 2014; and
- Was on the electoral roll for Canterbury electorates

The Health Protection team at Community and Public Health were notified of cases of *L. longbeachae* infection by the Canterbury Health Laboratories. A Health Protection Officer then assigned a unique study ID to each case and made contact to arrange an interview time. At the time of interview, cases were informed of the study aims and asked if they agreed to participate in an extended interview. Cases were also asked if they were on the electoral roll for Canterbury electorates in order to ensure that they came from the same population as controls. Probable cases of *L. longbeachae* that were not confirmed serologically were excluded from the analysis.

2.2.2 Control selection

The procedure for control selection was set out in the Standard Operating Procedure: Control Recruitment and Data Collection (Appendix B).

Controls were selected from the electoral roll for Canterbury electorates. *L. longbeachae* Legionnaires' disease is a community-acquired infection, and a population-based sample was appropriate to ensure that controls came from the population as cases (43). It was acknowledged that control recruitment from the general population is challenging and that there was a risk of a lower response rate than if hospital-based controls had been used, however, population controls were chosen with the aim of achieving a representative control sample.

Three hundred and one potential controls were randomly selected from the electoral roll for Canterbury electorates. The control sample was frequency matched by age within 10-year bands to past cases from 2008-2012 in order to achieve an age distribution among controls that approximated the expected age distribution of cases. The age distribution of past cases and the control sample is shown in Table 3 (Peter Mitchell, personal communication).

Table 3. Age distribution of past cases and control sample

Age group	Cases 2008-12		Control sample	
	n	%	N	%
30-39	4	4.5	14	4.7
40-49	7	7.9	24	8.0
50-59	18	20.2	61	20.3
60-69	30	33.7	101	33.6
70-79	21	23.6	71	23.6
80-89	8	9.0	30 (80+)	10.0
90+	1	1.1		
Total	89		301	

The control recruitment process consisted of three attempts to contact potential participants, two by mail and one by telephone, in order to maximise response rates (44). All potential controls were sent a letter (Appendix C) inviting them to participate in the study, along with an information sheet (Appendix D) outlining the study aims, a consent form (Appendix E), and a return addressed postage-paid envelope. Non-responders were followed-up with a second letter (Appendix F) approximately two weeks later, and then with a telephone call if there was no response to the second letter and a listed telephone number could be found.

The list of potential controls was randomly sorted into three groups and contacted in three stages. The intention of this approach was to keep pace with the volume of cases and recruit controls as near as possible to the time of interview. It was also anticipated that it might not be necessary to make contact with all three groups in order to recruit a sufficient number of controls to satisfy the ratio of three controls to one case. Control recruitment and interviews were tracked and monitored using a secure Microsoft Excel spreadsheet.

Controls who agreed to participate were assigned a unique study ID and contacted by telephone to arrange a time for a telephone interview. Interviewers first asked four health questions to screen participants prior to commencing the full interview. Controls were excluded from participating if they reported having symptoms of fever, cough, diarrhea, or chest pain lasting more than 24 hours within the previous three weeks in order to minimize the possibility of including undiagnosed cases of Legionnaires' disease.

2.3 Data collection

2.3.1 Questionnaire

A structured questionnaire (Appendix G) was used to collect the same information from both cases and controls, apart from the initial exclusion questions, which differed for each group. The questionnaire was developed with input from the steering group following a review of the literature on *L. longbeachae* infection and local surveillance data from recent years. The review identified a broad range of possible personal and environmental risk factors for *L. longbeachae* infection to be included in the questionnaire.

The questionnaire included 98 questions and covered the topics of garden environment; gardening and watering frequency and practices; recent exposure to soil, compost, and potting mix; hygiene practices related to gardening; and host features including demographic characteristics, pre-existing health conditions and smoking history.

A three-week reference period was used for all questions about exposures to allow for the approximate 2-14 day incubation period for *L. longbeachae* infection. This was applied as three weeks prior to the interview for controls and three weeks prior to becoming unwell for cases. The three-week reference period provided additional time beyond the incubation period to allow for any delay between the onset of infection, the appearance of symptoms, and admission to hospital for cases. This differed from the four-week reference period used in the South Australian study.

2.3.2 Interviews

The procedures for collecting information from cases and controls were set out in the Standard Operating Procedure: Control Recruitment and Data Collection (Appendix B)

and Standard Operating Procedure: Case Recruitment and Data Collection (Appendix A). These were drafted in August 2013 and finalized in September. Five interviewers were involved in undertaking case and control interviews throughout the study period.

Three designated Health Protection Officers (HPOs) from Community and Public Health were selected from among those who routinely follow-up cases of Legionnaires' disease to carry out all interviews with *L. longbeachae* cases during the study period. Three HPOs were needed to undertake case interviews in order to ensure that an interviewer was available to follow-up cases within a short timeframe throughout the week and during on-call periods, such as evenings and weekends and during the Christmas holidays, if necessary. Case interviews were usually conducted by telephone; however, in some instances it was necessary to interview cases in person in hospital due to the nature of their illness. The HPOs also collected samples of commercial potting mixes or composts recently used by cases for testing if any remained in the original packaging. If samples were being collected, the interview sometimes occurred at the same time at the cases' home.

Confirmed controls were contacted sequentially beginning from the top of the original, randomly ordered recruitment list once they had agreed to participate. Controls were not individually matched to cases; however, attempts were made to align the rate and timing of control interviews to that of cases as closely as possible. Interviews were conducted over the telephone by the study coordinator and two additional interviewers, both of whom were also designated HPOs. One of the HPO interviewers conducted both control and case interviews during the study period.

All interviewers were skilled and experienced, and additional measures were taken to ensure consistency of approach. The questionnaire was reviewed and discussed in detail

with each interviewer, then piloted and refined prior to the beginning of the study period. The study coordinator also observed other interviewers to check that questions were interpreted and delivered in a consistent manner.

2.3.3 Data entry

The responses from all interviews were recorded on hard copies of the questionnaire and entered into a secure Microsoft Excel spreadsheet throughout the data collection period. At the conclusion of data collection, the complete set of questionnaire responses was re-entered into a separate spreadsheet by another individual. The two data sets were compared using STATA 13 to identify discrepancies and the paper questionnaires were consulted to determine the correct values. A master data set was created to ensure accuracy of the data before analysis commenced.

The questionnaire and data spreadsheet contained the study ID and no other identifying information about the participants.

2.4 Analysis

This section outlines the approach to analyzing the study data. It should be noted that the initial analysis plan was based on a predicted sample size of 40 cases and this was adapted to support the final sample size of 21 cases.

2.4.1 Descriptive analysis

Descriptive analysis included response rates for cases and controls, and response patterns and times for controls in relation to the first letter, second letter, and telephone call. The descriptive analysis also included the characteristics of both groups on the basis of age

and sex, smoking history, and health status including pre-existing respiratory illness, cardiac illness, diabetes, and immunosuppression.

2.4.2 Univariate analysis

Univariate analysis included a selection of variables from the questionnaire that fell into three main areas: consideration of univariate analysis from the South Australian case-control study; analysis of additional variables of interest identified in the literature review; and analysis of combined variables that brought together two or more individual variables in order to address key risk factor groupings or scenarios. Each of these parts of the analysis is described in more detail below. Logistic regression was used in STATA 13 to calculate univariate odds ratios, 95% confidence intervals and p-values, with a significance level of 0.05.

Variables from South Australian study

Analysis of important variables identified in the South Australian study was replicated in this study. Odds ratios were calculated for the following variables made up of host risk factors and environmental exposures:

a. Pre-existing cardiac illness or respiratory illness
b. Smoking status and history (having ever smoked and having smoked for more than 30 years)
c. Recent exposure to commercially manufactured potting mix
d. Being near dripping hanging pots or baskets
e. Eating or drinking while gardening before washing hands

Analysis of these variables was modified to accommodate differences in study design. Logistic regression was used to calculate univariate odds ratios, rather than conditional

logistic regression, which was used in the South Australian study due to individual matching of cases and controls.

Additional variables

Additional univariate analysis was undertaken using logistic regression to calculate odds ratios for other potential risk factors identified in the literature review, including:

f. Other pre-existing health factors, including immunosuppression
g. Smoking history (having smoked for more than 10 years, 20 years)
h. The presence of indoor and outdoor gardens on the property
i. Gardening frequency, both indoors and outdoors
j. Garden watering practices
k. Recent exposure to homemade and commercially manufactured compost
l. Handling practices related to potting mix and compost
m. Smoking while using potting mix or compost before washing hands
n. Protective factors including use of facemask and gloves during potting mix use

This thesis focuses specifically on gardening-related risk factors and some questions in the questionnaire, such as those about having pets, exposure to dust, and other activities or features of the property, were not included in the scope of the analysis.

Combined variables

The final element of univariate analysis involved combining similar variables into themes. This was undertaken to assist with understanding risk at a practical level by illustrating several scenarios in which potting mix and compost is used. Univariate analysis was undertaken using logistic regression for the following combined variables:

a. Garden type on the property (indoor and outdoor) and frequency of gardening activity both indoors and outdoors

b. Exposure to purchased compost or potting mix were analysed together for all exposure-related variables due to the similarity of the content and manufacturing process for these products
c. Any behaviour that results in potting mix or compost being near the face (smoking, eating or drinking, or touching face after using potting mix or compost before washing hands)
d. Moving potting mix or purchased compost, either with hands or tipping or troweling

2.4.3 Stratified analysis

A second univariate analysis of potting mix and exposure stratified by smoking history was undertaken to determine the impact of long-term smoking on disease risk among users of compost-based products.

2.4.4 Multivariable analysis

Multivariable models

The investigators initially planned to replicate the multivariable models used in the South Australian case-control study and identify the strongest independent risk factors for illness from among the important host and environmental risk factors. It was advised, however, that multivariable models would statistically support one additional variable per 10 case observations, in additional to the outcome variable of *L. longbeachae* infection (C. Cameron, personal communication). The final sample size of 21 cases therefore allowed for models of at most three variables, including the outcome variable, which made replication of the South Australian models impossible. Instead, a multivariable model was designed using the most important host risk factor and environmental risk

factor identified in univariate analysis in order to determine the independent effect of each of these variables.

Confounding

Two additional multivariable models were designed to test for confounding. The first considered the possibility that pre-existing respiratory disease may confound the relationship between smoking history and Legionnaires' disease by including these two variables in a model with the outcome variable. The second model included recent exposure to potting mix or purchased compost, having an indoor garden, and developing *L. longbeachae* infection, as it was thought that exposure to potting mix or purchased compost may confound the relationship between having an indoor garden and Legionnaires disease if these participants were more likely to have used these products in the past three weeks.

Had the sample been larger, age would also have been added to all multivariable models in order to test for residual confounding despite frequency matching of cases and controls in ten-year age bands.

3 Results

This chapter presents the study results beginning with response rates for the case and control groups and participant characteristics, and then progressing through the findings of descriptive, univariate, stratified, and multivariable analysis. The results of descriptive and univariate analysis are broken down into host risk factors and environmental risk factors for *L. longbeachae* infection. The final section contains the results of multivariable analysis considering the independent effect of important risk factors and the role of confounding.

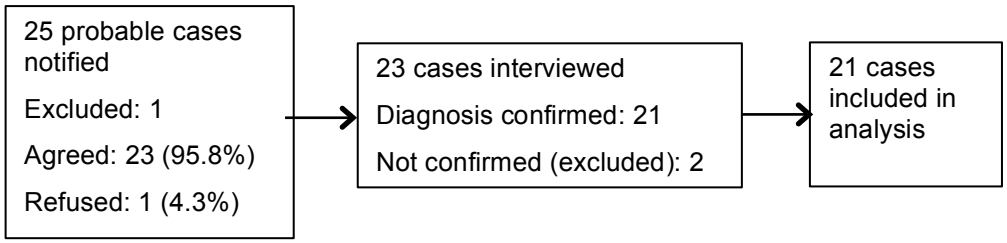
3.1 Response rates and sample size

The final study group included in the analysis consisted of 21 cases and 69 controls, achieving the desired ratio of three controls per case. The number of cases was substantially lower than the predicted figure of 40 cases used for sample size calculations during planning.

3.1.1 Case response

Figure 1 below depicts the process of case recruitment.

Figure 1. Case response flow chart

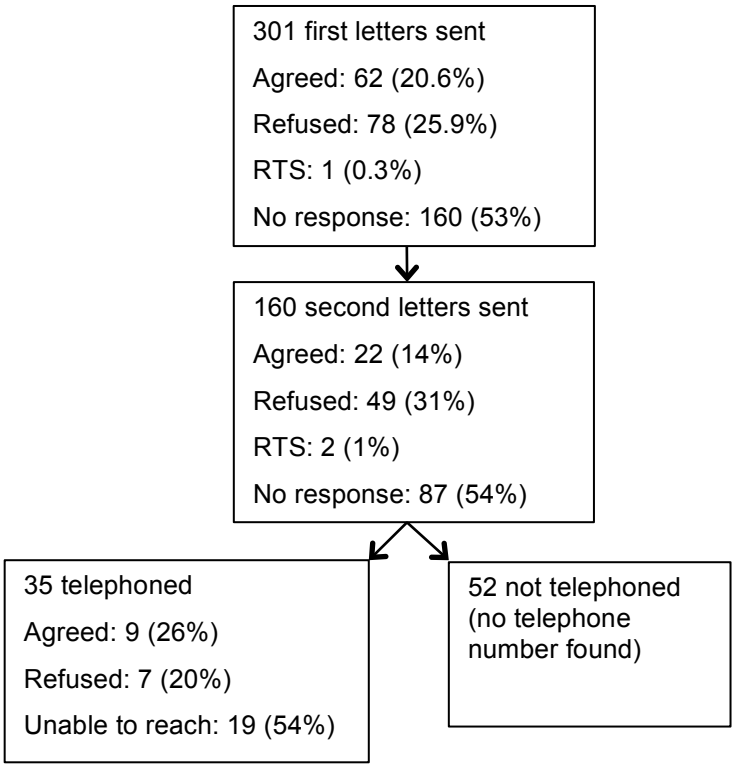


25 cases of *L. longbeachae* Legionellosis with an estimated disease onset between 1 October 2013 and 31 March 2014 were notified to Community and Public Health. One case resided outside of Canterbury and was excluded due to not being on the electoral roll for Canterbury electorates. One case refused to participate in the study, yielding an overall response rate of 95.8%. 23 cases were interviewed and two were later excluded from inclusion in the analysis when *L. longbeachae* infection was not confirmed diagnostically. This resulted in a total of 21 cases included in the study.

3.1.2 Control response

Figure 2 depicts the control recruitment process.

Figure 2. Control response flow chart

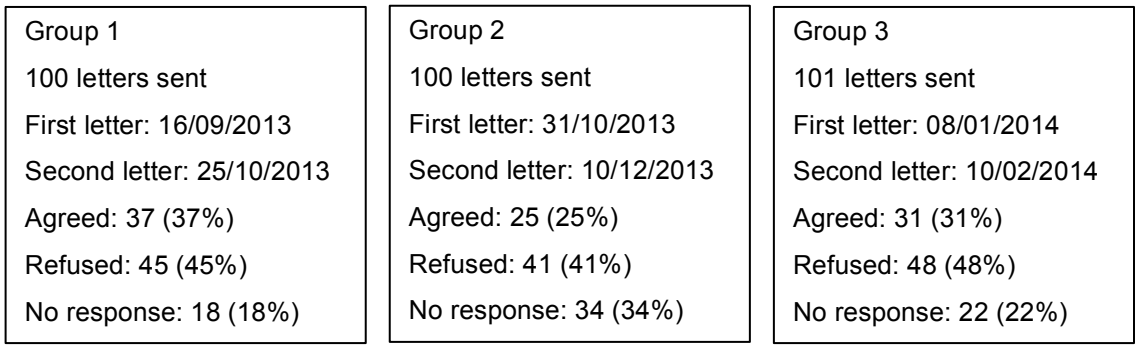


Letters were sent to all 301 potential controls throughout the study period. Overall, 93 (31%) potential controls agreed to participate in the study, 134 (45%) refused, and 77 (26%) did not respond and could not be contacted, including three letters that were returned to sender (RTS). This resulted in an overall a cooperation rate of 41% based on those who responded.

Control recruitment was undertaken in three groups throughout the study period, with each group receiving up to three attempts to contact the individual. Potential controls that did not respond to the first letter received a second letter approximately two weeks later, and those who did not respond the second letter received a telephone call if a contact telephone number could be found. Of those who agreed to participate, 62 (66.7%) responded to the first letter, 22 (23.7%) responded to the second letter, and nine (9.7%) agreed upon being called.

Figure 3 displays how response rates varied across the three recruitment groups in terms of acceptance, refusal, and no response.

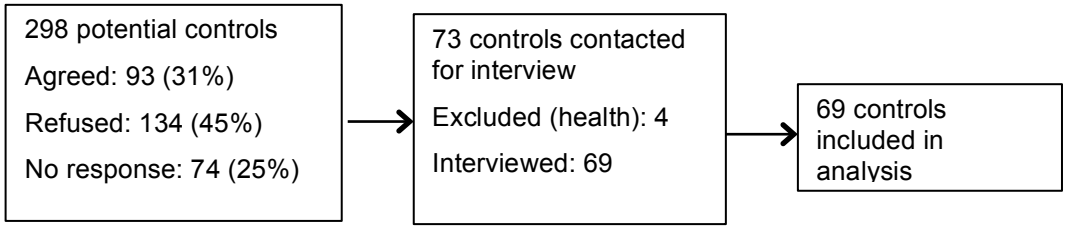
Figure 3. Response from each group of potential controls



Control interviews

Of the 93 controls that agreed to participate, 73 were contacted to arrange an interview. Four controls were excluded due to recent symptoms and 69 controls were interviewed to achieve a three to one ratio of controls to cases. Figure 4 depicts the control interview process.

Figure 4. Control interview flow chart



The number of control interviews completed was based on the original number of 23 cases prior to two cases being excluded following interview when diagnosis of *L. longbeachae* infection was not confirmed. Despite the surplus of controls available for interview, a decision was made not to exceed the three to one control to case ratio in order to optimize use of resources while carrying out the data collection. This approach was supported by statistical advice received during planning that a control to case ratio larger than three to one would not increase the power of the study (C. Cameron, personal communication).

Table 4 shows the distribution of control interviews in relation to case onsets and control interview targets for each period based on the three to one control-case ratio. Most cases were notified during the first half of the study period and numbers dropped off dramatically after January. Control interviews initially did not keep pace with case onsets, and then remained more constant throughout the study period to eventually meet and then exceed the desired three to one control to case ratio.

Table 4. Case onsets and control interviews

	Case onsets	Control interview target (3:1 ratio)	Control interviews
1 October – 30 November	10	30	25
1 December – 31 January	8	24	23
1 February – 31 March	3	9	21
Total	21	63	69

3.2 Participant Characteristics

Overall 21 cases and 69 controls were included in the study. The demographic characteristics of both groups are summarised in Table 5. The proportion of male cases (57.1%) was slightly higher than that of male controls (50.7%). A test of proportions showed that the difference in proportion of males between the two groups was not statistically significant (p=0.606).

Table 5. Demographic characteristics of cases and controls

	Cases		**Controls**	
Age				
range	47-88		33-86	
mean	68.48		66.61	
median	70		68	
	n	**%**	**n**	**%**
Number	21		69	
Sex				
male	12	57.1	35	50.7
female	9	42.9	34	49.3
Ethnicity				
NZ European	20	95.2	64	92.8
Maori	0	0.0	2	2.9
Other*	1	4.8	1	1.5
Household Income				
<$15,000	3	14.3	3	4.4
$15,001-$40,000	9	42.9	22	31.9
$40,001-$70,000	4	19.1	15	21.7
$70,001-$100,000	2	9.5	8	11.6
$100,001-$150,000	2	9.5	6	8.7
>$150,001	1	4.8	6	8.7

*Those who specified other reported their ethnicity as “British”.

The case and control groups had similar age structures due to frequency matching of the electoral roll extract to past cases in 10-year age bands. The cases were slightly older, with a mean age of 68.5 compared to 66.6 for controls. A two-sample t-test showed that the difference in mean age between the two groups was not statistically significant (p=0.455). The age range was also wider for the control group, with an age difference of 14 years between the youngest control and the youngest case interviewed. Table 6 shows the age distribution of cases and controls in each age group.

Table 6. Participants by age group

Age group	Cases		Controls	
	n	%	n	%
30-39	0	0.0	1	1.5
40-49	2	9.5	5	7.3
50-59	3	14.3	9	13.0
60-69	6	28.6	25	36.2
70-79	7	33.3	21	30.4
80-89	3	14.3	8	11.6
90+	0	0.0	0	0.0

3.3 Descriptive and univariate analysis

Descriptive analysis of all identified variables was undertaken to compare the prevalence of certain characteristics and exposures among cases and controls. The results are included in the tables below alongside the results of univariate analysis. This format assists with presenting results for variables for which there may have been too few observations to support the calculation of univariate odds ratios due to the small sample size for the study.

Logistic regression was used to calculate univariate odds ratios for variables of interest. As discussed in the Methods chapter (Section 2.4), the approach to univariate analysis

considered those factors found to be associated with disease in the South Australian case-control study as well as other potential risk factors identified in a review of literature. Results with a 95% confidence interval that did not include 1.0 and a p-value < 0.05 were deemed to be statistically significant.

Sample size calculations for the study were based on an expectation of 40 cases, and the smaller than expected final sample of 21 cases limited the scope of the analysis and led to some changes to the initial analysis plan. In two cases, multiple variables were combined to create new composite variables for particular measures in order to increase the power and broaden the scope of the analysis. This was undertaken for variables relating to garden environment and gardening frequency (presented in Table 9), and for variables considering the use of both potting mix and purchased compost (presented in Table 13) due to the similarity of these products.

The results have been separated into two categories: host risk factors, which relate to intrinsic characteristics of participants, such as health status and smoking history; and exposure risk factors relating to modifiable environmental exposures and gardening practices.

All descriptive and univariate results presented in the tables below are based on inclusion of the entire study group, except where otherwise noted. This study focused specifically on gardening-related risk factors. More information was collected from participants on several additional variables, not all of which are presented here.

3.3.1 Host risk factors

Table 7 and Table 8 show the results of the descriptive and univariate analysis of personal characteristics of case and control participants, including pre-existing health conditions, smoking status, and smoking history.

Table 7. Pre-existing health conditions

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Cardiac	7	33.3	17	24.6	1.53	0.53-4.41	0.432
Respiratory	6	28.6	12	17.3	1.90	0.61-5.90	0.267
Asthma	5	23.8	10	14.5	1.84	0.55-6.16	0.321
COPD	3	14.3	2	2.9	5.58	0.87-35.99	0.070
Diabetes	3	14.3	3	4.3	3.67	0.68-19.73	0.130
Immunosuppression	3	14.3	4	5.9	2.71	0.55-13.22	0.218
Other	12	57.1	42	60.9			

Cases were more likely than controls to have pre-existing health conditions, particularly respiratory illness, which was present in 28.6% of cases compared to 17.3% of controls. Cases were also more likely to suffer from pre-existing cardiac illness, diabetes, and immunosuppression. Univariate odds ratios did not, however, indicate increased risk of disease for any pre-existing health condition at levels of statistical significance.

Table 8. Smoking status and history

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Current smoker	4	19.0	5	7.2	3.01	0.73-12.45	0.128
Ever smoked	14	66.7	30	43.5	2.60	0.93-7.24	0.068
Smoked for 10 or more years	12	57.1	16	23.2	4.00	1.42-11.24	0.009
Smoked for 20 or more years	11	52.4	12	17.4	4.77	1.65-13.78	0.004
Smoked for 30 or more years*	9	42.9	10	14.5	4.05	1.35-12.12	0.012

*Reported in South Australian case-control study

Cases were more likely than controls to have ever smoked, be current smokers, or have smoked for long periods of time, although current smoking or having ever smoked were

not associated with disease in univariate analysis at levels of statistical significance. As in the South Australian study, having smoked for more than 30 years (OR 4.05, 1.35-12.12) was associated with disease. Further analysis of smoking duration revealed that having smoked for 10 or more years (OR 4.00, 1.42-11.24) was also strongly associated with *L. longbeachae* infection and appeared to increase disease risk to a similar level as having smoked for 20 or 30 years. There does not appear to be a dose-response relationship between duration of past smoking and risk of infection, with similar odds ratios for those who had smoked for 10, 20 and 30 years.

3.3.2 Exposure risk factors

Analysis of possible risk factors relating to environmental exposures considered the characteristics of the garden environment, gardening frequency, exposure to potentially contaminated products, and participant behaviour when gardening. The tables below present the results of both descriptive and univariate analysis of several variables, including those which were found to be associated with *L. longbeachae* infection.

Garden environment

Table 9 presents results relating to the garden environment of study participants. A similar proportion of cases (100%) and controls (97.1%) reported having an outdoor garden on the property, and it was not possible to calculate an odds ratio for this variable due to all cases having an outdoor garden.

Table 9. Garden environment

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Outdoor garden on property	21	100.0	67	97.1			
Indoor garden on property	7	33.3	8	11.6	3.81	1.18-12.27	0.025
Hanging pots or baskets on property	7	33.3	27	39.1	0.77	0.27-2.17	0.632
Near dripping hanging pots or baskets	2	9.5	15	21.7	0.38	0.08-1.82	0.224
Watered the garden or pot plants in the past three weeks	28	85.7	59	85.5	1.01	0.25-4.10	0.981

Those who reported having an indoor garden (a glass or tunnel house, conservatory, or hydroponics) on the property were at increased risk of *L. longbeachae* infection (OR 3.81, 1.18-12.27).

The presence of hanging pots or baskets on the property (OR 0.77, 0.27-2.17) and having been near dripping hanging pots or baskets (OR 0.38, 0.27-2.17) during the three-week reference period were not associated with disease in this study, as had been observed in the 1996-98 South Australian case-control study. Having watered the garden or pot plants in the three-week reference period (OR 1.01, 0.25-4.10) was also not associated with *L. longbeachae* infection.

Gardening frequency

Analysis of recent gardening activity and gardening frequency is shown in Table 8. Overall the prevalence of gardening during the three-week reference period was similar among cases (90.5%) and controls (91.5%).

Table 10. Gardening frequency

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Gardened in the past three weeks	19	90.5	63	91.3	0.90	0.17-4.86	0.907
Spent any time gardening outdoors	18	85.7	63	91.3	0.57	0.13-2.51	0.459
Spent any time gardening indoors	5	23.8	23	33.3	0.63	0.20-1.91	0.412
Spent one or more hours per day gardening outdoors	12	57.1	49	71.0	0.54	0.20-1.49	0.237
Spent one or more hours per day gardening indoors	1	4.8	1	1.5	3.40	0.20-56.83	0.392

A greater proportion of cases (42.9%) than controls (29.0%) reported spending on average more than one hour per day gardening outdoors on the days that they gardened. Proportionally fewer cases (23.8%) reported spending any time gardening indoors than controls (33.3%), although this was based on a broader definition of indoor gardening that including tending to indoor potted plants. There was no statistically significant association between gardening and disease for any variable relating to gardening frequency, indoors or outdoors.

Table 11 presents the results of further univariate analysis that considered the garden environment and gardening frequency together for both outdoor and indoor gardens.

Table 11. Garden type and frequency

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Outdoor garden on property and spent any time gardening outdoors	12	57.1	48	69.6	0.58	0.21-1.59	0.293
Indoor garden on property and spent any time gardening indoors	4	19.1	5	7.25	3.01	0.72-12.45	0.128

The odds ratio for those who had an indoor garden and spent any time gardening indoors (OR 3.01, 0.73-12.45) indicates that this group may be at increased risk of *L. longbeachae* infection, however, this finding is not statistically significant.

Exposure to potting mix

The questionnaire was designed to examine exposure to soil, potting mix, and compost separately. The prevalence of gardening was nearly identical for cases and controls, and disease risk associated with soil exposure was not analysed since gardening inevitably involves exposure to soil. Table 12 reports the descriptive analysis and univariate odds ratios for potting mix use and several related behaviours. Reported use of potting mix during the three-week reference period increased disease risk (OR 3.71, 1.34-10.29).

Table 12. Potting mix exposure and behaviour

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Used potting mix in the last three weeks	13	61.9	21	30.4	3.71	1.34-10.29	0.012
Ate or drank after using potting mix before washing hands	4	19.1	1	1.5	16.00	1.68-152.54	0.016
Touched face after using potting mix before washing hands*	6	28.6	2	2.9	21.33	3.72-122.25	0.001
Smoked after using potting mix before washing hands	1	1.45	1	4.8	3.40	0.20-56.83	0.394
Any opportunity for potting mix near face (smoking, eating or drinking, or touching face)**	9	50.0	4	5.9	16.00	4.07-62.90	0.000
Wore gloves when using potting mix**	8	61.5	15	71.4	0.64	0.15-2.77	0.550
Wore a mask when using potting mix**	3	23.1	3	14.3	1.80	0.30-10.64	0.517
Aware of risks associated with potting mix use	11	52.4	22	31.9	2.35	0.87-6.56	0.092

*9 participants (3 controls and 6 cases) responded “Don’t know” to this question and were not included in this analysis.

**Analysis includes only those who reported using potting mix in the last three weeks (21 controls and 13 cases)

Eating or drinking after using potting mix before washing hands (OR 16.00, 1.63-152.54) was highly associated with disease. Touching the face after using potting mix before washing hands (OR 21.33, 3.72-122.25) was also strongly associated with *L. longbeachae* infection. Certainty in these findings is limited due to these analyses being based on very few exposed cases, resulting in extremely wide confidence intervals. The odds ratio for smoking after using potting mix before washing hands (OR 3.40, 0.20-56.83) was not statistically significant. Further analysis was undertaken to consider the combined risk for any activity that results in the opportunity for potting mix to come in contact with the face (eating or drinking, touching the face, or smoking), and these respondents were found to be at increased risk (OR 16.00, 4.07-62.90).

Possible protective factors considered in univariate analysis included wearing a mask and wearing gloves while using potting mix. This analysis included only those participants who reported using potting mix, rather than the entire study group, in order to determine the effect of using gloves or a mask among those exposed. Wearing a mask while using potting mix (OR 1.80, 0.30-10.64) did not appear to be protective against disease. Those who reported wearing gloves while using potting mix (OR 0.64, 0.15-2.77) were less likely to contract *L. longbeachae* infection than those who did not wear gloves, although this finding is not statistically significant. Awareness of the risks associated with potting mix (OR 2.35, 0.87-6.56) did not reduce disease risk.

Exposure to compost

Table 13 presents the analysis of variables relating to the use of homemade and purchased compost.

Table 13. Compost exposure and behaviour

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Used any compost (homemade or purchased)	11	52.4	28	40.6	1.61	0.60-4.30	0.341
Used purchased compost	10	47.6	14	20.3	3.57	1.26-10.08	0.016
Used homemade compost	2	9.5	16	23.2	0.35	0.07-1.66	0.186
Ate or drank after using any compost before washing hands	2	9.5	5	7.3	1.35	0.24-7.51	0.734
Ate or drank after using purchased compost before washing hands	2	9.5	3	4.4	2.32	0.36-14.88	0.376

Exposure to any compost (both purchased and homemade) during the three-week reference period was not associated with disease, however, use of purchased compost (OR 3.57, 1.26-10.08) was. Use of homemade compost did not increase disease risk (OR 0.35, 0.07-1.66). Those who ate or drank after using purchased compost before washing hands (OR 2.32, 0.36-14.88) were more likely to contract *L. longbeachae* infection than those who did not, although this finding is not statistically significant.

Exposure to potting mix or purchased compost

Due to the similarities in the content and manufacture of compost and potting mix products, and increased risk of infection among those who used either product, a further combined analysis was undertaken to consider exposure to purchased compost or potting mix exposure. Inclusion of both products also served to increase the power of the analysis for variables relating to gardening practices and behaviour, as presented in Table 14.

Table 14. Potting mix and purchased compost exposure and behaviour

	Cases N=21		Controls N=69		OR	95% CI	p-value
	n	%	n	%			
Used purchased compost or potting mix	16	76.2	30	43.5	4.16	1.37-12.64	0.012
Ate or drank after using purchased compost or potting mix before washing hands	4	19.0	4	5.8	3.82	0.87-16.88	0.077
Touched face after using potting mix or purchased compost before washing hands*	N=148	57.1	N=616	9.8	12.22	3.16-47.29	0.000
Smoked after using potting mix or purchased compost before washing hands	2	9.5	2	2.9	3.53	0.47-26.72	0.223
Any opportunity for potting mix or purchased compost near face (smoking, eating or drinking, or touching face)*	N=1711	64.7	N=649	14.1	11.20	3.31-37.92	0.000
Opened purchased compost or potting mix	13	61.9	18	26.1	4.60	1.64-12.92	0.004
Used purchased compost or potting mix indoors	3	14.3	2	2.9	5.58	0.87-35.99	0.070
Tipped or trowelled purchased compost or potting mix	15	71.4	23	33.3	5.00	1.71-14.59	0.003
Moved purchased compost or potting mix with hands	11	52.4	18	26.1	3.11	1.13-8.57	0.028
Moved potting mix or purchased compost around (with hands or by tipping/trowelling)	16	76.2	27	39.1	4.98	1.63-15.17	0.005
Wore a mask while using purchased compost or potting mix**	N=163	18.8	N=303	10.0	2.07	0.37-11.74	0.480
Wore gloves while handling purchased compost or potting mix**	N=169	56.3	N=3021	70.0	0.55	0.16-1.94	0.354

*Participants who responded "Don't know" were not included in the analysis.

**Analysis includes only those who reported using potting mix or purchased compost in the last three weeks (30 controls and 16 cases).

Use of potting mix or purchased compost (OR 4.16, 1.37-12.64) was associated with *L. longbeachae* infection. Touching the face after using potting mix or purchased compost before washing hands (OR 12.22, 3.16-47.29) was strongly associated with disease. A much higher proportion of cases (19.1%) than controls (5.8%) reported eating or drinking after using potting mix or purchased compost before washing hands, although the univariate odds ratio (OR 3.82, 0.87-16.88) for this analysis was not statistically

significant. Similarly, the odds ratio for smoking after using potting mix or purchased compost before washing hands (OR 3.40, 0.20-56.83) was not statistically significant. There was also a strong association with disease (OR 11.02, 3.31-37.92) for the combined analysis of any opportunity for potting mix or purchased compost to come in contact with the face (by smoking, eating or drinking, or touching the face while using these products).

Table 14 also presents the results for several more specific behaviours relating to the use of these products. Having opened purchased compost or potting mix (OR 4.6, 1.64-12.92) and having tipped or troweled purchased compost or potting mix (OR 5.00, 1.71-14.5) were strongly associated with disease. Moving potting mix or purchased compost with hands (OR 3.11, 1.13-8.57) was also associated with disease. Increased risk was also found in a combined analysis of variables relating to handling or moving these products around (OR 4.98, 1.63-15.17).

Wearing a mask while using potting mix or purchased compost (OR 2.07, 0.37-11.74) did not appear to be protective against disease. Those who reported wearing gloves while using potting mix or purchased compost (OR 0.55, 0.16-1.94) were less likely to contract *L. longbeachae* infection than those who did not wear gloves, although the univariate odds ratio was not statistically significant. As with the potting mix analysis presented in Table 9, analysis of possible protective factors included only those participants who reported using potting mix or purchased compost, rather than the entire study group, in order to determine the effect of using gloves or a mask among those exposed.

3.3.3 Stratified analysis

The strongest predictors of illness in univariate analysis were having smoked for 10 or more years and use of potting mix or purchased compost during the 3-week reference

period. Further analysis of potting mix and purchased compost exposure stratified by long-term smoking status was undertaken to evaluate the relationship between these two important variables and *L. longbeachae* infection.

Table 15. Smoking history and use of potting mix or purchased compost

	Cases		Controls		OR	95% CI	p-value
	n	%	n	%			
Neither used purchased compost or potting mix nor smoked 10+ yrs	3	14.3	27	39.1	1.00*		
Used purchased compost or potting mix (only those who had smoked 10+yrs)	10	47.6	7	10.1	6.43	1.05-39.33	0.044
Used purchased compost or potting mix (only those who had not smoked 10+yrs)	6	28.6	21	30.3	2.57	0.57-11.51	0.217
Smoked for 10+yrs and did not use purchased compost or potting mix	2	4.7	9	13.0	2.00	0.29-13.94	0.484

* reference group

Table 15 shows that the increased risk to users of potting mix and purchased compost who had also smoked for 10 or more years (OR 6.43, 1.05-39.33) was much greater than that for those users who had not smoked for 10 or more years (OR 2.57, 0.57-11.51) and that for smokers who had not used potting mix (OR 2.00, 0.29-12.94).

3.4 Multivariable analysis

3.4.1 Multiple risk factors

During planning of the study, it was anticipated that multivariable analysis would be used to try to replicate the multivariable models used in the South Australian case-control study and identify the strongest independent risk factors for illness from among the important host and environmental risk factors. However, the small sample size limited

this planned approach. Based on biostatistical advice that multivariable models could validly support one variable additional to the outcome variable of *L. longbeachae* infection per 10 case observations (C. Cameron, personal communication), the final sample size of 21 cases allowed for models with at most two exposure variables. The plan to replicate the main multivariable model used in the South Australian case-control study, which included five variables, was not possible. At the time analysis was carried out for this study, a decision had been made to proceed with a second season of data collection (separate from this thesis) due to the low number of cases. More sophisticated multivariable analysis was deferred until both seasons of data could be considered together. However, stratified analysis and two three-variable multivariable models to test for possible confounding were carried out to expand upon the findings of univariate analysis.

3.4.2 Opportunities for confounding

The multivariable models presented below were designed to focus on host or exposure risk factors in order to test for possible scenarios of confounding. Multiple regression was used to determine if the inclusion of two variables to the model produced odds ratios that were substantially different from the corresponding univariate odds ratios.

Smoking history and pre-existing respiratory disease

The first multivariate model relates to the association between smoking history and pre-existing respiratory disease, and the impact this relationship may have on the observed outcome of *L. longbeachae* infection associated with these factors. It was considered that smoking may confound the relationship between pre-existing respiratory disease and

Legionnaires' disease, if the respiratory illness was associated with smoking but not on the causal pathway.

Table 16. Smoking history and pre-existing illness

	Crude		Adjusted		p-value
	OR	95% CI	OR	95% CI	
Smoked for 10 or more years	4.00	1.42-11.24	3.89	1.37-10.99	0.01
Pre-existing respiratory illness	1.90	0.61-5.90	1.76	0.52-5.87	0.36

As shown in Table 16, the inclusion of pre-existing respiratory disease and having smoked for more than 10 years in a multivariable model did not substantially alter the odds ratio for pre-existing respiratory disease (OR 1.76, 0.52-5.87), suggesting that it is unlikely that smoking history acted as a confounder in this case.

Having an indoor garden and exposure to potting mix

As presented earlier, having an indoor garden (OR 3.81, 1.18-12.27) was associated with disease in univariate analysis, although this was not the case for having spent any time gardening indoors (OR 0.63, 0.20-1.92). It was thought that recent potting mix or purchased compost use may act as a confounder in the relationship between having an indoor garden and developing *L. longbeachae* infection, if those with an indoor garden were more likely to have used potting mix or purchased compost in the past three weeks.

Table 17. Indoor garden and exposure to potting mix

	Crude		Adjusted		p-value
	OR	95% CI	OR	95% CI	
Indoor garden on property	3.81	1.18-12.27	3.00	0.89 - 10.13	0.077
Used potting mix or purchased compost in the past 3 weeks	4.16	1.37-12.64	3.60	1.16 - 11.20	0.027

Table 17 shows that when having an indoor garden is adjusted for recent use of potting mix or purchased compost in a multivariable model, the odds ratio for having an indoor garden (OR 3.00, 0.89-10.13) remains similar to the unadjusted value, however, the confidence interval is wider and drops below one.

4 Discussion

This chapter presents a summary of key findings of the case-control study and relates these findings to previous research and epidemiological investigation of *L. longbeachae* Legionnaires' disease. Discussion of the findings in the first section of the chapter is categorized in terms of host risk factors, exposure risk factors, protective factors, and factors that illustrate possible modes of transmission of bacteria from the environment to humans.

The second section is a critical appraisal of the study, presenting the strengths and limitations of the study design, opportunities for bias and confounding, and possible implications for interpretation of the results.

Summary of results

The findings show that older people, those with pre-existing illness, and those who have smoked for 10 or more years are at increased risk of *L. longbeachae* infection. A history of long-term smoking is a key risk factor for illness. Important environmental risk factors include exposure to commercially manufactured and potting mix and compost, behaviour that transfers these products directly to the mouth or face, poor hand hygiene during gardening, and using these products in a way that agitates the material to produce dust. Using these products indoors may also increase risk. The results indicate that transmission of bacteria from the environment to humans may occur through ingestion or inhalation of contaminated particles. Water does not appear to be an important factor in the transmission process. Reported use of a mask does not appear to reduce risk, although the sample was too small to consider the impact of variation in mask type and use.

Reported use of gloves reduced risk in the study group, although not at levels of statistical significance.

4.1 Findings in the context of previous research

This study found that history of long-term smoking was associated with *L. longbeachae* infection and may be an important risk factor. Long-term smokers who used potting mix were much more likely to get sick than non-smokers and those who smoked for less than 10 years who used these products. Current and past smoking status were not associated with illness. Pre-existing illness and immunosuppression were also not associated with increased risk of disease at levels of statistical significance.

Having an indoor garden and having recently used potting mix or purchased compost were associated with disease. Several more specific practices relating to the use of potting mix or purchased compost, specifically those that resulted in these materials getting near the face and mouth, were also highly associated with illness, suggesting that handling and use may have an impact on level of infection risk.

4.1.1 Host risk factors

The case-control analysis of host risk factors considered several personal characteristics that were thought to make some individuals more susceptible to *L. longbeachae* Legionnaires' disease. Review of disease surveillance information and published literature on *L. longbeachae* infection, and risk factors for Legionnaires' disease and community-acquired pneumonia generally, suggested that age, pre-existing health conditions, and smoking status and history may have an impact on disease risk. This

section provides a discussion of the findings of this study in each of these areas, in relation to available information on these factors and previous research.

Demographic characteristics

The mean age of cases in the study of 68.5 and age range of 47-88 is consistent with information that suggests that older age increases disease risk. The mean age of cases in the study was similar to that of cases in the South Australian case-control study (1) as well as disease surveillance information for recent *L. longbeachae* cases in Canterbury (8) (4) and Scotland (25) (39).

As discussed in the Methods chapter, the list of potential controls for the study was frequency matched by age in 10-year age bands to past cases as part of the study design in order to recruit a more age-appropriate control group. Due to this, it was not possible to perform a case-control analysis of age to assess if this is an independent risk factor for illness. The relationship between age and disease risk is likely to be influenced by other intrinsic factors, such as pre-existing illness and smoking history, which are discussed in more detail below.

The proportion of male cases (57.1%) was slightly higher than that of male controls (50.7%), which is consistent with previous research and suggests that males may be at greater risk of disease than females. An assessment of demographic differences between the case and controls groups for the study, and implications for the results, is presented in the Critical Appraisal section of this chapter.

Pre-existing health conditions

Cases were more likely than controls to have pre-existing health conditions, including respiratory illness, cardiac illness, diabetes, and immunosuppression. This finding is consistent with available information on risk factors for Legionellosis and community-acquired pneumonia more generally (38). 28.6% of cases reported having pre-existing respiratory disease compared to 17.3% of controls. Among those with respiratory disease, 14.3% of cases had COPD compared to 2.9% of controls resulting in a univariate odds ratio of 5.58, although this analysis was based on a very small number of exposed cases and was not statistically significant. While the results of descriptive analysis suggest that poor health may be a risk factor for *L. longbeachae* infection, univariate analysis did not indicate increased risk of disease for any pre-existing health condition at levels of statistical significance. This differed from the South Australian case-control study, which found that both pre-existing cardiac illness (OR 7.29, 1.52-34.98) and respiratory illness (OR 17.62, 2.15-144.25) were strongly associated with *L. longbeachae* infection. Both studies had small sample sizes and the confidence intervals for these odds ratios in the South Australian study were very wide, which reduces certainty in what can be concluded from the findings. Further analysis with a larger sample, potentially including multiple seasons of data, would assist with determining if those in the general population with specific types of pre-existing illness are likely to be at increased risk of contracting Legionnaires' disease.

Smoking status and history

Smoking was highlighted as an important risk factor for *L. longbeachae* infection in both descriptive and univariate analysis. Cases were more likely than controls to have ever smoked, be current smokers, or have smoked for long periods of time. Being a current

smoker or having ever smoked were not individually associated with disease in univariate analysis, as was observed in the South Australian case-control study. Having smoked for more than 30 years (OR 4.05, 1.35-12.12), however, was associated with disease. Further analysis of past smoking duration revealed that having smoked for 10 or more years (OR 4.00, 1.42-11.24) was also strongly associated with *L. longbeachae* infection, increasing disease risk to a similar level as having smoked for 20 or 30 years. The results show that smoking history is an important risk factor for illness, which is consistent with existing knowledge of risk factors for community-acquired pneumonia (38, 40).

4.1.2 Exposure risk factors

Exposure risk factors differ from host risk factors in that they are largely modifiable environmental or behaviour-related activities that may increase or decrease risk of disease. Information on exposure risk factors may assist with developing the existing body of knowledge on the type of media that are likely to be affected by bacterial contamination and possible modes of disease transmission. A better understanding of behaviour or environmental factors that potentially increase risk or provide protection against illness would also assist with the development of health promotion measures to reduce the burden of illness in the community.

Garden environment and gardening frequency

There was a very high prevalence of gardening in both the control group (91.3%) and the case group (90.5%). This may have been due to a high prevalence of gardening among the general Canterbury population, or possibly due to the inclusion of the study aims in the control recruitment information, the possible implications of which are discussed in more detail later in this chapter in a critical appraisal of the study design. Similarly,

97.1% of controls reported having an outdoor garden at their property, compared to 100% of cases as shown in Table 4. Due to these similarities between the case and control groups, it was not possible to determine if gardening, having an outdoor garden per se, or use of soil were individual risk factors for *L. longbeachae* infection in univariate analysis. There was also no statistically significant association between frequency of gardening outdoors and disease.

Indoor gardening was identified as a possible risk factor for Legionnaires' disease in the review of the literature on *L. longbeachae* infection. In this study, those who reported having an indoor garden (a glass or tunnel house, conservatory, or hydroponics) on the property were found to be at increased risk of disease (OR 3.81, 1.18-12.27) in univariate analysis. There was, however, no statistically significant association between gardening indoors and disease when considering those who spent any time gardening indoors and those who spent one or more hours per day gardening indoors (see Table 10). Univariate analysis that included both having an indoor garden and having gardened for one or more hours per day indoors (OR 3.01, 0.73-12.45) indicated that this group may be at increased risk of developing Legionnaires' disease, however, this finding was not statistically significant.

A potential limitation of the findings relating to indoor gardening presented in Tables 9-11 may have arisen due to the wording of the questions regarding indoor gardening, which included 'tending to or watering indoor potted plants' as a form of indoor gardening and therefore did not distinguish between this form of casual gardening inside a dwelling and spending time in a confined indoor garden space, such as a glass house, tunnel house or hydroponics operation. This limitation is discussed in greater detail later in this chapter in section 4.2.1 Study design.

It is also possible that participants who had an indoor garden were more likely to have recently used potting mix or commercially-manufactured compost than those who only have an outdoor garden. If this was the case, the observed association between having an indoor garden and *L. longbeachae* infection may have been confounded by potting mix and compost use. A multivariable model was used to consider the relationship between having an indoor garden, use of potting mix or commercially manufactured compost in the past three weeks, and *L. longbeachae* infection. The results in Table 10 show that the association between having an indoor garden is very similar to the univariate odds ratio presented in Table 9. While it is not possible to rule out that the univariate result is due to confounding, as discussed later in section 4.2.4, indoor gardening appears to be an independent risk factor for illness.

Exposure to potting mix and purchased compost

Identifying modifiable exposure risk factors for *L. longbeachae* infection was an objective of the study. Due to the isolation of *L. longbeachae* from some widely-used soil products and the known association between exposure to these products and *L. longbeachae* infection, the questionnaire and analysis looked extensively at exposure and behaviour related to the use of soil, compost and potting mix products. Key findings of the study were that reported use of potting mix during the three-week reference period increased disease risk, as did exposure to purchased compost.

When specific behaviours or activities relating to potting mix exposure were considered independently, eating or drinking and touching the face after potting mix use before washing hands greatly increased disease risk over exposure alone. A limitation of these findings is the small number of observations included in the analysis, leading to wide confidence intervals and less certainty in the validity of the results. The results do,

however, highlight the importance of conducting further research into hygiene-related issues and the potential risks associated with transferring contaminated products to the mouth or face. This is discussed later in 4.1.4 Modes of transmission.

A further combined analysis considered exposure to purchased compost or potting mix due to the similarities between these products. Inclusion of both purchased compost and potting mix also increased the power of the analysis for variables relating to gardening practices and behavior, allowing for a more detailed analysis of these variables than for potting mix or compost exposure alone.

4.1.3 Impact of multiple risk factors

Stratified univariate analysis

The stratified analysis revealed that smoking history modified the effect of recent exposure to potting mix or commercial compost on *L. longbeachae* infection. Users of potting mix and purchased compost who had a history of smoking for 10 or more years (OR 6.43, 1.05-39.33) were at much greater risk of developing *L. longbeachae* Legionnaires' disease than those users who had not smoked for 10 or more years (OR 2.57, 0.57-11.51). Importantly, the odds ratio for the non-10 year smoker strata was not statistically significant, with the lower limit of confidence interval dropping below the null value. This reinforces the importance of smoking history as an independent factor for *L. longbeachae* infection.

4.1.4 Protective factors

Possible protective factors considered in univariate analysis included wearing a mask and wearing gloves while using potting mix. Consistent with the findings of the South

Australian study, wearing a mask while using potting mix (OR 1.80, 0.30-10.64) did not appear to be protective against disease. Those who reported wearing gloves while using potting mix (OR 0.64, 0.15-2.77) were less likely to contract *L. longbeachae* infection than those who did not wear gloves, although this finding is not statistically significant. Unlike the South Australian study, awareness of the risks associated with potting mix (OR 2.35, 0.87-6.56) did not reduce disease risk.

4.1.5 Modes of transmission

The primary mode or modes of transmission of *L. longbeachae* bacteria from environmental sources to humans are not well understood. Previous epidemiological research points to several possible transmission modes. The questionnaire for this case-control study was designed to gather more information on this topic for three particular topic areas: water-related transmission, transfer of contaminated material to the face or mouth, and exposure to airborne contaminated material.

Water-related transmission

An environmental exposure that was associated with illness in the South Australian case-control study was being near dripping hanging pots or baskets. Access to ferneries was also noted during *L. longbeachae* case-control study in South Australia (1). It was hypothesized that transmission from potting mix may occur through inhalation or aspiration of aerosolised contaminated water, and that this process was aided due to baskets hanging at head height (37).

The questionnaire for the Canterbury case-control study included specific questions about the presence of hanging pots and baskets in the garden environment, and recent exposure

to hanging pots or baskets that were dripping water. Having hanging pots or baskets on the property and having been near dripping hanging pots or baskets were not associated with disease in this case-control study. Having watered the garden or indoor plants during the reference period was also not associated with illness in this study. These findings do not support the hypothesis that transmission occurs through exposure to *L. longbeachae* contaminated water.

Further questions were also asked about watering methods used in the garden, such as hand-held watering or use of irrigation systems, frequency of watering, and recent exposure to watering either at home or at another location, with the intention of determining if there was an association between watering and disease. The sample size for the study was not sufficient to undertake more detailed analysis of watering practices, although this information may be useful if further analysis is undertaken including multiple seasons of data.

Transfer of contaminated material to the face or mouth

A second proposed mode of transmission considered in the case-control analysis was ingestion or inhalation of potentially contaminated material transferred directly to the mouth or face. The South Australian case-control study found an association between eating and drinking after using potting mix without washing hands and *L. longbeachae* infection.

This study also found that eating or drinking and touching the face after potting mix use before washing hands greatly increased disease risk over exposure to potting mix alone. Further analysis was undertaken to consider the combined risk for any activity that results in the opportunity for potting mix to come in contact with the face (eating or drinking,

touching the face, or smoking), and these respondents were also found to be at increased risk (OR 16.00, 4.07-62.90). It is acknowledged that the confidence intervals for these odds ratios are very wide due to the study's small sample size. Repeating these analyses with multiple seasons of data would provide greater certainly of the results.

The combined variables for potting mix and purchased compost also showed that getting these products on or near the face increases disease risk. Touching the face after using potting mix or purchased compost before washing hands (OR 12.22, 3.16-47.29) was strongly associated with disease. Similarly, a much higher proportion of cases (19.1%) than controls (5.8%) reported eating or drinking after using potting mix or purchased compost before washing hands, although the univariate odds ratio (OR 3.82, 0.87-16.88) for this variable was not statistically significant. Moving potting mix or purchased compost with hands (OR 3.11, 1.13-8.57) was also associated with disease. The combined analysis considering all three of these factors together (OR 11.02, 3.31-37.92) found that potting mix or purchased compost being near the face may put users at greater risk than use of potting mix or purchased compost alone. This supports the theory that users become infected by inhaling or ingesting contaminated material.

Exposure to airborne contaminated material

A third suspected mode of transmission is through the inhalation of dust aerosols containing *L. longbeachae* bacteria (18). It is thought that users may be at increased risk when contaminated material is agitated and expelled into the air as dust. To consider this mode, participants were asked if they had opened purchased compost or potting mix, tipped or trowelled purchased compost or potting mix, or moved it with their hands.

The case-control analysis found that having opened purchased compost or potting mix (OR 4.6, 1.64-12.92) and having tipped or troweled purchased compost or potting mix (OR 5.00, 1.71-14.5) were more strongly associated with disease than exposure alone. Moving potting mix or purchased compost with hands (OR 3.11, 1.13-8.57) was also associated with disease. Increased risk was also found in a combined analysis of variables relating to all three of the above variables around handling or moving these products around (OR 4.98, 1.63-15.17). These findings support the suggestion that dust may play an important role in the disease transmission process.

4.2 Critical appraisal

This section provides a discussion of the strengths and limitations of the study. The critical appraisal considers study design, response rates and sample size, and potential sources of bias and confounding.

4.2.1 Study design

A population-based case-control study was the most appropriate and efficient design for this research project. *L. longbeachae* Legionnaires' disease is a rare infection affecting a very small proportion of the population. Unlike other designs, a case-control study makes use of all identified cases within a defined population during a specified time period. This maximises the study sample size and power to detect associations between exposures and disease.

Participant selection and recruitment

The opportunity to work directly with the public health unit and make use of the existing notifiable disease process to identify and interview cases was a strength of the study.

Using this approach, a high case response rate of over 95% was achieved with only one case refusing to participate in the study. Case ascertainment is also likely to have been very high, as it is unlikely that any hospitalised cases of *L. longbeachae* Legionnaires' disease were missed due to routine PCR testing of all hospitalised pneumonia patients in Canterbury.

Voting enrolment is compulsory in New Zealand, and use of the electoral roll to select controls increased the likelihood that the resulting control group would be representative of the general population. A limitation of using population controls, however, is the risk of low response rates, which was experienced in this study and is discussed further in section 4.2.2. An alternative to this approach is the use of pre-agreed controls, such as an existing group similar to that used in the South Australian study that had previously participated in other studies. Advantages of this include the likelihood of a higher response rate, more information about non-responders, and the ability to individually match cases and controls by age. The key limitation of this approach, however, is the introduction of systematic bias due to the control group not being representative of the general population. *L. longbeachae* Legionnaires' disease is a community-acquired infection and, despite the potential challenges, it was felt that electoral roll recruitment was more likely to produce an internally valid sample and therefore more accurate and useful results.

Data collection

Due to the use of Health Protection Officers in the public health unit to follow up cases, it was necessary for multiple interviewers to be involved in data collection for cases and controls. Three HPOs were involved in interviewing cases, and only one of these interviewers had additional capacity to interview controls. In total, six interviewers

undertook case and control interviews. Five were designated HPOs with experience in notified disease follow-up and the sixth was myself, a postgraduate public health student and study coordinator. While there is potential for multiple interviewers to introduce variation in the interview approach, this was controlled through the development of Standard Operating Procedures for data collection, training of all interviewers, piloting and refinement of the study questionnaire prior to beginning of the study period, and moderation during the early interviewing process undertaken by the study coordinator.

The same questionnaire was used for cases and controls in order to minimise variation in data collection for the two groups. Some differences in when and how cases and controls were interviewed were unavoidable. The cases involved in the study had all recently been unwell and most were admitted to hospital. All control interviews were conducted over the phone, however, some cases were interviewed in person if they were still in hospital or recently discharged. HPOs were also required to collect samples of potting mix or compost for testing from cases if available, making a home visit a more convenient method of undertaking the interview. While it is possible that these different modes of interviewing participants may have introduced variation in the way participants responded to questions, it is not likely to have had a major impact on the data quality due to use of a standardised questionnaire and small team of experienced interviewers.

The timing of case and control interviews, presented in Table 1, is another factor that should be taken into account when considering the comparability of the responses received from the two groups. Control interviews were scheduled as cases were notified in an attempt to align the distribution of case and control interviews throughout the study period. Despite this, most cases were notified during the first half of the study period and the rate at which control interviews were scheduled and completed initially did not keep

pace to achieve the three to one control to case ratio for the period from 1 October through 30 November. Case numbers dropped off substantially after January, with only three cases being notified from 1 February through 31 March, while the rate of control interviews remained relatively constant throughout this period. The difference in the number of control interviews conducted during each phase of the study period from the three to one target was not statistically significant; however, more precise timing would have ensured that factors not specifically considered in the questionnaire, such as weather conditions and seasonal changes, had minimal impact.

Questionnaire limitations

Some limitations of the questionnaire were identified during the interview process and analysis. It was recognized during analysis that the definitions of an 'indoor garden' and 'indoor gardening' were inconsistent in the questionnaire, limiting the analysis of these two variables. When participants were asked if they had an indoor garden on their property in question 2, this was defined as a "glass or tunnel house, hydroponics operation, or conservatory." When asked about time spent gardening indoors in question 9, however, this was described in much more broad terms as "in an enclosed space or tending to indoor potted plants." While analysis of question 2 demonstrated that having an indoor garden increased disease risk, the broad definition of indoor gardening meant that it was not possible to assess if those who had spent time gardening in a true indoor garden environment were more likely be infected than those who mainly gardened outdoors. This would have been avoided by having consistent definitions for indoor and outdoor gardens and gardening.

A further limitation of the questionnaire was the lack of consideration for the state of potting mix and purchased compost being used. Interviewers noted informally that both

cases and controls sometimes commented on the moisture content of these products when purchased and opened, which ranged from dry and dusty to sopping wet. This information may have been useful due to the lack of certainty around how *L. longbeachae* is transmitted from environmental sources to humans, and hypotheses of water or dust-related transmission processes. Some respondents also mentioned that they had used bulk free-flowing potting mix or compost rather than bagged. It is unclear if *L. longbeachae* is equally likely to inhabit bagged and un-bagged products, and with a large enough sample this information may have been useful to determine if either situation poses a greater risk.

4.2.2 Response rates and sample size

As mentioned earlier, the high level of case ascertainment and a high case response rate of over 95% were strengths of the study. Despite this, the study was restricted by a smaller than anticipated sample size. The small sample of only 21 cases limited the scope of univariate analysis and made multivariable analysis unfeasible. The explanation for the lower than expected number of notified cases during the 2013-2014 *Legionella* season is unknown, however the number of cases does vary from year to year (3), and there may have been an impact of increased publicity about Legionnaires' disease and/or public health campaigns promoting safe handling of potting mix.

Univariate odds ratios for some variables were based on very few exposed cases or controls, resulting in extremely wide confidence intervals and less certainty in the results. The small sample size also meant that multivariable analysis was not well supported and it was not possible to attempt to replicate the multivariable models used in the South Australian study.

Control recruitment from the general Canterbury population also proved challenging. It was anticipated that the electoral roll list of 301 potential controls would be more than sufficient to recruit the expected number of 120 controls needed to provide a three to one ratio of 40 cases were notified. Despite having a much smaller final sample of only 21 cases, all 301 potential controls were contacted yielding a positive response rate of 31% and cooperation rate of 41% out of those who replied to the invitation to participate. Of the 93 potential controls who agreed to participate in the study, 73 were contacted to schedule interviews in an attempt to keep time with case onsets and interview three controls per case. As discussed in the Results chapter, the surplus controls were not interviewed in order to optimize use of resources as it was advised that exceeding the three to one ratio would not increase the power of the study appreciably. This is not likely to be a source of bias as controls were contacted at random throughout the study period.

An interesting feature of control recruitment was the high refusal rate—people taking the time to respond to the letter but declining the invitation to participate. It is not possible to know if or how the control group differed from the general population due to limited information on non-responders. One possibility is that the inclusion of the study aims and reference to gardening in the recruitment materials for controls led those who did not have an interest in gardening to decline to participate or not respond. This would result in a higher prevalence of gardening in the control group than in the general population, and therefore a greater level of exposure to the risk factors of interest in the study such as having a garden, having gardened recently, and having been exposed to potting mix or compost. The equally high level of prevalence of gardening among cases (90.5%) and controls (91.3%) supports this theory, however, no data of gardening prevalence in Canterbury could be found to confirm whether or not this level of gardening is representative of the Canterbury population. If anything, this difference would serve to

underestimate the associations between exposure to these risk factors and *L. longbeachae* infection. While it is not possible to rule out that responders differed from non-responders in other ways, it is unlikely that the odds ratios observed in this study, many of which are large in magnitude, are entirely a result of non-response bias.

It was also thought that perhaps the ongoing disruption caused by the Canterbury earthquakes might have caused potential controls to be less inclined to take part. A separate project was carried out later in 2014 to assess population response rates to a similar invitation from four major New Zealand centres; Auckland, Wellington, Christchurch, and Dunedin (P. Priest, personal communication). Response rates were comparable across the four centres and similar to that of the Legionnaires' disease case-control study, suggesting that this level of participation is not unique to Canterbury.

4.2.3 Potential for bias

Selection bias

Despite frequency matching by age, controls were slightly younger overall, with an age range of 33-86 and mean age of 66.6, compared to a range of 47-88 and mean of 68.5 for cases. Table 3 shows that the age structure of the case and control group is similar overall, and it is unlikely that the age difference had an impact on the prevalence of risk factors in the control group.

As discussed in section 4.2.2, there is a possibility that controls differ from the general population in terms of gardening prevalence due to knowledge of study aims. It is possible that those who had an interest in gardening and the risks associated with Legionnaires' disease were more likely to agree to participate. The study aim of considering the association between Legionnaires' disease and activities such as

gardening was intentionally included in recruitment materials for controls in order to replicate as closely as possible the prior knowledge of cases and controls when they were asked to participate and at the time of interview. Cases were aware that the interview related to their recent illness as part of the disease surveillance process. The impact of selection bias favouring gardeners would be the underestimation of odds ratios for gardening-related risk factors due to control having greater exposure to gardening-related risk factors than the source population.

Information bias

Poor recall among cases is a potential source of bias for the study. Although the same reference period of three weeks was used for cases and controls, this was effectively a longer time period for cases as they were asked to report activity that occurred during the three weeks prior to when they became unwell as opposed to the three weeks immediately prior to the time of interview, as was the case for controls. The fact that most cases had been critically unwell and hospitalised between the reference period and interview also increased the likelihood of recall bias. The three-week reference period was chosen taking into consideration the 2-14 day incubation period for *Legionella* infection and potential delay between disease initiation and appearance of remembered symptoms resulting in cases. A two-week reference period may have been sufficient, and possibly more effective in terms of accuracy of recall.

Another form of recall bias that may have affected information collected from cases relates to recollection of behaviour. Cases were aware that they were being interviewed as part of the notifiable disease surveillance process, and it is possible that they may have, either intentionally or unintentionally, underreported or over-reported behaviour perceived to be risky or irresponsible, such as smoking or eating and drinking while using

potting mix before hand washing. Underreporting would lead to underestimation of the associations between these exposure and disease. Over-reporting would result in the overestimation of these associations, however, it is unlikely that this form of bias would have occurred consistently enough to explain the size of the odds ratios observed across many variables in the study.

4.2.4 Potential for confounding

Smoking history and pre-existing respiratory disease

Few opportunities for confounding were identified. Due to the known association between smoking and respiratory disease, it was thought that smoking history may confound the observed relationship between respiratory disease and *L. longbeachae* infection. The inclusion of pre-existing respiratory disease and having smoked for more than 10 years in a multivariable model did not substantially alter the association between pre-existing respiratory disease and *L. longbeachae* infection, suggesting that it is unlikely that smoking history acted as a confounder.

Having an indoor garden and exposure to potting mix

As presented earlier, having an indoor garden was associated with disease in univariate analysis, although this was not the case for having spent any time gardening indoors. It was thought that potting mix use may act as a confounder in the relationship between having an indoor garden and developing *L. longbeachae* infection, if those with an indoor garden were more likely to have used potting mix in the past three weeks. When recent potting mix exposure and having an indoor garden are included in a multivariate model, the association between having an indoor garden (OR 3.33, 0.98-11.25) and disease is no

longer statistically significant, although the lower limit only just drops below 1.0. This suggests that the univariate analysis may have been confounded by recent potting mix use to some degree, but this is not conclusive.

4.2.5 Concluding remarks

The study findings demonstrate the existence of statistically significant associations between both host risk factors and gardening-related risk factors and *L. longbeachae* infection. While the study was robustly designed and had several strengths, the small case sample size and low control response rate were notable limitations. Repeating the analysis with a larger sample made up of two or more seasons of data is necessary to increase certainty in the results.

5 Conclusion

This concluding chapter of the thesis provides a review of the aims and objectives of the thesis, discusses the implications of the findings, and sets out recommendations for public health practice and future research into *L. longbeachae* Legionnaires' disease.

5.1 Thesis review

The aim of this thesis was to improve understanding of risk factors for Legionnaires' disease caused by *L. longbeachae* in Canterbury. This was achieved by carrying out a review of background information and epidemiological research on Legionnaires' disease and conducting a case-control study of *L. longbeachae* infection during the 2013-2014 *Legionella* season.

Host risk factors

The first objective of the study was to investigate host risk factors for Legionellosis caused by *L. longbeachae*, including demographic characteristics, health status, and smoking history. The results highlighted that long-term smoking is an important risk factor for disease, and that a history of smoking for 10 or more years further increases risk for those exposed to potting mix and purchased compost. Long-term smokers, whether current or past, should be advised to exercise extreme caution when using these products. Pre-existing health issues may also be important although this aspect of the findings was inconclusive and should be studied further with a larger sample.

Environmental risk factors

The second objective was to investigate environmental risk factors for Legionellosis and possible modes of transmission of *L. longbeachae* bacteria from environmental sources to humans. Important environmental risk factors include exposure to commercially manufactured potting mix and compost, behaviour that transfers these products to the mouth or face, poor hand hygiene after gardening, and using these products in a way that agitates the material to produce dust. Using compost-based products indoors may also increase risk. The findings suggest that transmission of bacteria from the environment to humans may occur through ingestion or inhalation of contaminated particles, although water does not appear to be an important factor in the transmission process.

Preventive measures

The third objective was to evaluate the effectiveness of existing measures recommended to prevent Legionellosis, such as wearing gloves or a mask when handling potentially contaminated materials. Reported use of a mask did not reduce risk in the study, although the sample was too small to consider the impact of variation in mask type and use. Based on the findings discussed above, however, it is possible that inappropriate use of a mask that results in potting mix or compost getting on or near the face, such as reusing a mask, removing or readjusting the mask while using potting mix or compost, or not washing hands after mask removal, would counteract any protective affect afforded by mask use.

Reported use of gloves reduced risk in the study group, although not at levels of statistical significance. As with mask use, wearing gloves without also taking necessary precautions to prevent potentially contaminated products from coming in contact with the face or mouth is unlikely to reduce risk. Keeping potting mix and compost away from the face

appears to be a key measure for preventing Legionnaires' disease, and it is important that recommendations relating to mask and glove use reinforce this issue.

5.2 Recommendations

The fourth and final objective of the study was to develop recommendations based on the findings relating to health promotion messaging for disease prevention and future epidemiological research into *L. longbeachae* Legionellosis in Canterbury and further afield. In relation to disease prevention, I recommend that:

1. Public health messages relating to potting mix and compost use clearly state the increased risk of disease for those with a history of long-term smoking, not just current smokers, and the importance of safe handling of potting mix and purchased compost for these users;
2. Public health messages relating to disease prevention emphasize the importance of keeping potting mix or compost residue away from the face and mouth; and
3. Public health messages relating to mask and glove use reinforce the above principle (such as by promoting appropriate use of single-use disposable masks) and the importance of hand-washing after use

In relation to future research, I recommend that:

4. The Canterbury case-control study is repeated with a larger sample that includes one or more additional seasons of data, in order to:
5. Determine with greater certainty the impact of particular important host risk factors, such as smoking history and pre-existing health conditions, on disease risk;
6. Consider the association between indoor gardening or use of potting mix or compost indoor and disease; and

7. Consider behaviour relating to mask and glove use in more detail to determine if these preventive measures in fact decrease disease risk for those who use potting mix and compost

At the time of submission of this thesis, the case-control study has already been extended to include an additional study period from October 2014-March 2016, and preliminary findings of the two-season study are being prepared for publication.

Finally, in relation to continuing epidemiological research into *L. longbeachae* Legionnaires' disease in New Zealand and internationally, I recommend that:

8. Testing strategies are put in place in conjunction with disease surveillance processes to routinely test for Legionella species other than *L. pneumophila* in order to determine the prevalence and disease burden of *L. longbeachae* infection

At the time of submission of this thesis, a one-year Health Research Council funded study of rolling out the Canterbury testing strategy New Zealand-wide was currently under way (D. Murdoch, personal communication).

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Appendices

Appendix A. Standard Operating Procedure: Case Recruitment and Data Collection

Case-control study of risk factors for *L. longbeachae* Legionnaires' disease in Canterbury, New Zealand

Standard Operating Procedure: Case Identification and Data Collection
This Standard Operating Procedure has been written to provide guidance for identifying cases of *L. longbeachae* Legionnaires' disease for inclusion in the case-control study, and to establish the interview process in order to ensure consistency of data collection methods.

Case Selection

Inclusion Criteria

Legionnaires' disease is a notifiable disease and cases will be identified and interviewed by Health Protection Officers (HPOs) at Community and Public Health (CPH), a division of the Canterbury District Health Board. This will occur in conjunction with the normal process for following up all cases of *L. longbeachae* Legionnaires' disease notified during the study period of 1 October 2014 and 31 March 2015. CPH is notified of cases by Canterbury Health Laboratories following detection of *L. longbeachae* in patient samples. All notified cases are eligible for inclusion in the case-control study, except those who meet the exclusion criteria below.

Exclusion Criteria

Controls from the general Canterbury population will be recruited from the electoral roll. Cases not listed on the electoral roll for Canterbury will be excluded from the study to ensure that cases and controls come from the same population. The case questionnaire includes a screening question to establish this prior to proceeding with the interview. If the case is not on the electoral role, the HPO will revert to the routine questionnaire for Legionellosis cases.

Study ID

Each case will be assigned a study ID consisting of the letters 'CA' and two digits, beginning with '01' and numbered sequentially. The Study ID will be assigned by the Communicable Diseases Duty Person on the page in the duty folder upon initial notification of the case, and will be recorded on the completed interview template. No other identifying information will be included on the questionnaire form.

Case interviews
HPOs should familiarise themselves with the questionnaire prior to making the phone call to the case. If there are any queries they should speak to Kate, Debbie or Fiona who completed them last summer. If the case matches the inclusion criteria and they agree to take part the questions should be read as they are written and the appropriate response recorded. If the questionnaire is unable to be completed by the actual case

(e.g. they are intubated) then record who is completing the questionnaire at the top of the front page i.e. wife
Generally the questionnaire will be carried out during normal working hours, however, if a case prefers to complete the questionnaire after hours then a thorough handover to the On call HPO will be required including providing an overview of the questionnaire. On call staff will also need to complete the questionnaire during the Christmas/New year period where possible.

Information provided to cases

Standardised information (included on the case questionnaire form) will be provided to cases about the information being collected in the interview. The HPO conducting the interview will explain that CPH are collecting additional information from people with Legionnaires' disease this summer in order to gain a better understanding of who is affected by the disease and why, in order to prevent future cases from occurring. If, after providing this information and responding to questions, there is any uncertainty about the participants' willingness to provide the requested information, the HPO will revert to the regular to Legionellosis questionnaire.

Interview process

Interviews will occur over the phone if possible, however, it may be necessary for some interviews to occur in person either in the hospital or in the home. If the case is acutely unwell or deceased, the HPO may endeavour to complete the interview with an immediate family member if it is deemed appropriate.
The Case Questionnaire form is stored electronically in CFS and blank hard copies of the form are in the *Legionellosis* drawer of the communicable disease cabinet. Prior to starting the interview, the HPO will record the Study ID, interviewer name, interview date and time on the top of the questionnaire form. The HPO will conduct the interview according to instructions, sequence of questions, and skip logic set out on questionnaire form. Responses should be recorded on a printed hard copy version of the questionnaire and provided to Debbie Smith for forwarding to the study coordinator Pippa Scott at Otago University.

Storage

Completed hard copies of the questionnaire form will be forwarded to the study coordinator and be kept in a locked filing cabinet.

Appendix B. Standard Operating Procedure: Control Recruitment and Data Collection

Case-control study of risk factors for *L. longbeachae* Legionnaires' disease in Canterbury, New Zealand

Standard Operating Procedure: Control Recruitment and Data Collection
This Standard Operating Procedure (SOP) has been written to provide guidance for recruiting control participants for the case-control study, and to establish the interview process in order to ensure consistency of data collection methods.

Control Selection

Inclusion Criteria

300 potential controls have been randomly selected from the electoral roll for Canterbury. The only parameter for the electoral roll request was frequency matching by age to past cases in 10-year age bands.

Recruitment

The list of 300 potential controls will be divided into three groups of 100, and recruitment will occur in three six week cycles in an effort to make contact with controls as closely as possible to the time of interview. All potential controls will be sent a letter inviting them to participate in the study, an information sheet, and a consent form. Non-responders will be followed up with a second letter approximately two weeks later, and then with a telephone call if a listed telephone number can be located.

Study ID

Each control will be assigned a study ID consisting of the letters 'CO' and three digits, beginning with '001' and numbered sequentially as potential controls respond and agree to participate in the study. The study ID will be assigned by study coordinator upon receipt of a signed consent form and will be recorded in the Control spreadsheet.

Exclusion Criteria

At the time of interview, controls that have experienced an episode of diarrhoea, fever, chest pain, or cough lasting more than 24 hours within the past three weeks will be excluded from the study. The intention of these criteria is to exclude potential undiagnosed cases of Legionnaires' disease. The control questionnaire includes an eligibility question covering these symptoms.

Control Interviews

All control interviews will be undertaken over the telephone by the study coordinator or supporting interviewer using the Control Questionnaire form. The supporting interviewer will be familiarised with the questionnaire and complete a trial interview prior to the beginning of the study to identify and address and issues.

Information provided to controls

Standardised information (included on the Control Questionnaire form) will be provided to all controls about the information being collected and structure of the interview.

Interview process

Once a control has agreed to participate and been assigned a study ID, the study coordinator or supporting interviewer will contact the control by telephone to arrange an interview time. Controls will be contacted in sequential order from the top of the recruitment list working down.

The Control Questionnaire is stored electronically in CFS. Prior to starting the interview, the interviewer will record the study ID, interviewer name, interview date and time on the top of a hard copy of the questionnaire form. No other identifying information will be included on the form.
The interviewer will conduct the interview according to instructions, sequence of questions, and skip logic set out on questionnaire form. Responses should be recorded on a printed hard copy version of the questionnaire and provided to the study coordinator (Emma Kenagy) for data entry as soon as possible following the interview.

Storage

Completed hard copies of the questionnaire form will be stored by the study coordinator in a locked filing cabinet.

Appendix C. Control recruitment letter

«Date»

«AddressBlock»

«GreetingLine»

You have been randomly selected from the electoral roll to be invited to take part in a study that is being undertaken by the University of Otago in partnership with the Canterbury District Health Board.

The study is about summer activities, such as gardening, and possible links with Legionnaires' disease, and would involve a telephone interview. We need to speak to people who do not have Legionnaires' disease to compare their experiences with people who have had the disease. We would greatly appreciate your participation, even if you do not do any gardening.

Please read the enclosed information sheet for more details about the study. If you agree to take part, sign and return the consent form in the postage paid envelope provided. We will get in touch with you to organise a time for a telephone conversation over the next few months. You can also let us know your decision by emailing **study@cdhb.health.nz**. If you do not wish to participate, please let us know so that we do not contact you again.

Thank you for taking the time to read the information provided. Please do not hesitate to contact one of the people listed on the information sheet if you have any questions.

Kind regards,

Prof David Murdoch
Department of Pathology
University of Otago
Christchurch

Dr Patricia Priest
Department of Preventive and Social Medicine
Dunedin School of Medicine
University of Otago

Emma Kenagy
Community & Public Health
Canterbury District Health Board

Appendix D. Control information sheet

Participant Information Sheet

Study title: **Study of Gardening Activity and Legionnaires' Disease**

Principal investigator: Prof David Murdoch, Department of Pathology, University of Otago Christchurch, ph (03) 364 0590

Introduction

Thank you for showing an interest in this project. Please read this information sheet carefully. Take time to consider and, if you wish, talk with relatives or friends before deciding whether or not to participate.

If you decide to participate we thank you. If you decide not to take part there will be no disadvantage to you and we thank you for considering our request.

What is the aim of this research project?

This spring and summer the University of Otago and the Canterbury District Health Board will be undertaking a study to learn more about the risk factors for Legionnaires' disease in Christchurch. Legionnaires' disease is a type of pneumonia caused by bacteria commonly found in soil.

The purpose of the study is to increase our understanding of why some people get Legionnaires' disease and how to prevent those at risk from getting sick.

Participants from the general population without Legionnaires' disease are needed to provide details about gardening activity during the spring and summer period.

Who is funding this project?

This study is being undertaken by Emma Kenagy as part of a thesis for a Master of Public Health degree and is being partly funded by the Canterbury District Health Board.

Who are we seeking to participate in the project?

You have been randomly selected from the Electoral Roll and we would like to invite you to participate in the study.

If you participate, what will you be asked to do?

If you agree to participate, an interviewer will contact you by telephone at a pre-arranged time during the spring or summer to complete a questionnaire about your health and recent gardening activities. The interview will take approximately 30 minutes. We may also request to take some specimens of soil or compost from your garden, to be tested for the bacteria that cause Legionnaires' disease.

What about anonymity and confidentiality?

To ensure your privacy, all information provided to the interviewer will be treated confidentially and will be de-identified for the purposes of the study. The consent form, which has your name on it, will be stored separately from your questionnaire, which will be identified only with a number. These will be stored for five years following the study then destroyed.

If you agree to participate, can you withdraw later?

You may withdraw from participation in the project at any time and without any disadvantage to yourself.

Any questions?

If you have any questions now or in the future, please feel free to contact any of the following:

Prof David Murdoch Department of Pathology University of Otago Christchurch	Contact phone number: (03) 364 0590
Dr Patricia Priest Senior Lecturer, Epidemiology Department of Preventive and Social Medicine, Dunedin School of Medicine	Contact phone number: (03) 479 7204
Emma Kenagy Community & Public Health Canterbury District Health Board	Contact details: (03) 378 6858 027 567 1313 study@cdhb.health.nz

This study has been approved by the University of Otago Human Ethics Committee (Health); reference number H13/065. If you have any concerns about the ethical conduct of the research you may contact the Committee through the Human Ethics Committee Administrator (ph 03 479 8256). Any issues you raise will be treated in confidence and investigated, and you will be informed of the outcome.

Appendix E. Control consent form

Study of Gardening Activity and Legionnaires' Disease

Principal investigator: Prof David Murdoch
Department of Pathology
University of Otago Christchurch
ph (03) 364 0590

CONSENT FORM FOR PARTICIPANTS

Please review the enclosed INFORMATION SHEET for more information about the study and details of involvement if you choose to a participant.
Please return this form by post using the envelope provided.
Tick one:

☐ I agree to be a participant in the study.

Please also complete the other side of this page, and provide your contact details and signature, and witness signature.

☐ I do not wish to be involved in the study.

If this consent form is not signed and returned by post, we will follow up with you again by post and/or telephone, and verbal consent to participate may be sought by telephone. We will not contact you further if you indicate on the form or verbally that you do not wish to participate in the study.

Following signature and return to the research team this form will be stored in a secure place for five years.

Participant Contact Details

Name: «Title» «Forenames» «Surname»

Best contact telephone number:_____

1. I have read the Information Sheet concerning this study and understand the aims of this research project.
2. All my questions about the project have been answered to my satisfaction, and I understand that I am free to request further information at any stage.
3. I know that my participation in the project is entirely voluntary, and that I am free to withdraw from the project at any time.
4. I know that as a participant I will be contacted to arrange a time for a telephone interview during the spring or summer and some specimens of soil or compost from my garden may be requested, to be tested for the bacteria that cause Legionnaires' disease.
5. I know that when the project is completed all personal identifying information will be removed from the paper records and electronic files which represent the data from the project, and that these will be placed in secure storage and kept for at least five years. This consent form will be stored separately from the data.
6. I understand that the results of the project may be published and be available in the University of Otago Library, but that no personal identifying information will appear in any spoken or written report of the study.
7. I know that there is no remuneration offered for this study, and that no commercial use will be made of the data.

Signature of participant:	Date:

Signature and name of witness:	Date:

This study has been approved by the University of Otago Human Ethics Committee (Health), reference number H13/065. If you have any concerns about the ethical conduct of the research you may contact the Committee through the Human Ethics Committee Administrator (ph 03 479 8256). Any issues you raise will be treated in confidence and investigated and you will be informed of the outcome.

Appendix F. Control follow-up letter

«Date»

«AddressBlock»

«GreetingLine»

Last month we sent you a letter inviting you to take part in a study that is being undertaken by the University of Otago in partnership with the Canterbury District Health Board. As far as we know, we have not yet heard back from you about whether or not you would like to participate.

The study is about summer activities, such as gardening, and possible links with Legionnaires' disease. Participation involves a short telephone interview, as we need to speak to members of the general public who do not have Legionnaires' disease to compare their experiences with people who have had the disease. Your participation is of great value to the study, even if you do not do any gardening.

Please read the enclosed information sheet for more details. If you agree to take part, sign and return the consent form in the postage paid envelope provided. We will get in touch with you to organise a time for a telephone conversation over the next few months. You can also let us know your decision by emailing **study@cdhb.health.nz**. If you do not wish to participate, please let us know so that we do not contact you again.

Thank you for taking the time to read the information provided. Please do not hesitate to contact one of the people listed on the information sheet if you have any questions.

Kind regards,

Prof David Murdoch
Department of Pathology
University of Otago
Christchurch

Dr Patricia Priest
Department of Preventive and Social Medicine
Dunedin School of Medicine
University of Otago

Emma Kenagy
Community & Public Health
Canterbury District Health Board

CASE CONTROL STUDY OF LEGIONNAIRES' DISEASE **Study ID:**

CONTROL QUESTIONNAIRE

Appendix G. Questionnaire

Recruitment ID:

Study ID:

Interviewer:

Date and time of interview:

Eligibility

Interviewer: I will give you more information about the questionnaire in a moment but before we get started, I need to get some information about your recent health to find out if you're eligible to participate in the study.

In the past three weeks, have you experienced an episode lasting more than 24 hours of:

i. Diarrhoea	1 ☐ Yes	2 ☐ No	**[i.Diarrhoea]**
ii. Fever	1 ☐ Yes	2 ☐ No	**[ii.Fever]**
iii. Chest pain	1 ☐ Yes	2 ☐ No	**[iii.ChestPain]**
iv. Cough	1 ☐ Yes	2 ☐ No	**[iv.Cough]**

If the answer is yes to any of the above questions, the participant is excluded from the study.

If no, continue with the questionnaire.

Interviewer: *This questionnaire includes questions about your property and garden (if you have one), and the things you do while gardening (if you garden). There are also some basic health and personal questions at the end. Even if you don't have a garden or do any gardening, your answers will help us with our research.*

You are welcome to ask questions during the interview if you need clarification on a topic and you may refuse to answer any question. The interview time will vary but may take up to 30 minutes.

Do you have any questions before we get started?

Garden Environment

1. Do you have an outdoor garden at your property? **[1.OutGarden]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

CASE CONTROL STUDY OF LEGIONNAIRES' DISEASE **Study ID:**

CONTROL QUESTIONNAIRE

2. Do you have an indoor garden (glass/ tunnel house, hydroponics, conservatory)? **[2.InGarden]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

3. Do you have indoor pot plants? **[3.InPotPlant]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

4. Do you have outdoor pot plants? **[4.OutPotPlant]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

5. Do you have hanging pots or baskets? **[5.HangPotBask]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

Gardening Activity

6. Have you spent any time gardening in the past three weeks? **[6.Gard3Wks]**

1 ☐ Yes ➔ Go to 7

2 ☐ No ➔ Go to 15

88 ☐ Don't know

99 ☐ Refused

7. In the past three weeks, how many days per week did you garden on average? **[7.DaysWkGard]**

1 ☐ One to three

2 ☐ Four or more

88 ☐ Don't know

CONTROL QUESTIONNAIRE

99 ☐ Refused

8. On average, how many hours per day did you spend gardening outdoors (in open air) on the days you gardened? **[8.HrsGardOut]**

1 ☐ None
2 ☐ Less than one hour
3 ☐ One to three hours
4 ☐ Four or more hours
88 ☐ Don't know
99 ☐ Refused

9. On average, how many hours per day did you spend gardening indoors (in an enclosed space or tending to indoor pot plants) on the days you gardened? **[9.HrsGardIn]**

1 ☐ None
2 ☐ Less than one hour
3 ☐ One to three hours
4 ☐ Four or more hours
88 ☐ Don't know
99 ☐ Refused

10. Do you purchase plants or raise plants from seed, or both? **[10.PlantsSeed]**

1 ☐ Purchase seedlings or plants
2 ☐ Raise plants from seed
3 ☐ Both
88 ☐ Don't know
99 ☐ Refused

11. Do you grow produce (fruits or vegetables)? **[11.Produce]**

1 ☐ Yes ➔ Go to 12
2 ☐ No ➔ Go to 13
88 ☐ Don't know
99 ☐ Refused

12. Do you wash produce from the garden before eating? **[12.WashProduce]**

1 ☐ Yes, always
2 ☐ Sometimes
3 ☐ No

88 ☐ Don't know

99 ☐ Refused

13. In the past three weeks, have you received any cuts or abrasions while gardening? **[13.CutsAbrasions]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

14. In the past three weeks, have you gotten soil or dust in your eyes while gardening? **[14.SoilDustEyes]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

15. In the past three weeks, have you watered a garden or pot plants? **[15.Watered]**

1 ☐ Yes ➔ Go to 16

2 ☐ No ➔ Go to 18

88 ☐ Don't know ➔ Go to 18

99 ☐ Refused ➔ Go to 18

16. What method of watering was used? **[16.WaterMethod]**

1 ☐ Irrigation (sprinkler) ➔ Go to 18

2 ☐ Hand-held watering ➔ Go to 17

3 ☐ Both ➔ Go to 17

88 ☐ Don't know ➔ Go to 18

99 ☐ Refused ➔ Go to 18

17. How much time did you spend hand-held watering over the past three weeks? **[17.HrsWatering]**

1 ☐ Less than one hour

2 ☐ One to three hours

3 ☐ Four or more hours

88 ☐ Don't know

99 ☐ Refused

18. In the past three weeks, have you been near dripping hanging pots or baskets? **[18.DrpPotBask]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

19. In the past three weeks, have you visited a garden centre or nursery? **[19.GardCentre]**

1 ☐ Yes ➔ Go to 20

2 ☐ No ➔ Go to 22

88 ☐ Don't know ➔ Go to 22

99 ☐ Refused ➔ Go to 22

20. Was watering taking place during your visit to the garden centre? **[20.WtGrdCntr]**

1 ☐ Yes ➔ Go to 21

2 ☐ No ➔ Go to 22

88 ☐ Don't know ➔ Go to 22

99 ☐ Refused ➔ Go to 22

21. What method of watering was used? **[21.WtMthdGrdCntr]**

1 ☐ Irrigation (sprinkler)

2 ☐ Hand-held watering

3 ☐ Both

88 ☐ Don't know

99 ☐ Refused

22. Have you been near any other garden during watering during the past three weeks? **[22.OtherWater]**

1 ☐ Yes, specify _____ **[22a.SpecOtherWater]**

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

CONTROL QUESTIONNAIRE

23. Have you cleaned or cleared out any gutters or drains in the past three weeks? **[23.GutterDrain]**

1 ☐ Yes ➔ Go to 24

2 ☐ No ➔ Go to 25

88 ☐ Don't know ➔ Go to 25

99 ☐ Refused ➔ Go to 25

24. Did you use water (for example a hose or pressure washer) to clear the guttering/drain? **[24.WtrGutterDrain]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

25. Have you mowed grass in the past three weeks? **[25.MowGrass]**

1 ☐ Yes ➔ Go to 26

2 ☐ No ➔ Go to 27

88 ☐ Don't know ➔ Go to 27

99 ☐ Refused ➔ Go to 27

26. How many weeks had it been since you mowed previously? (if you mowed more than once in the last three weeks, think about the first time) **[26.PrvMowGrass]**

_____ weeks

27. Are there any bodies of water or water features on or bordering your property? **[27.BodyWater]**

1 ☐ Yes ➔ Go to 28

2 ☐ No ➔ Go to 29

88 ☐ Don't know ➔ Go to 29

99 ☐ Refused ➔ Go to 29

28. What type of water feature or body or water? **[28.WaterType]**

Specify: _____

CONTROL QUESTIONNAIRE

29. Do you have a bird feeder or put out food for birds in your garden? **[29.BirdFeeder]**

1 ☐ Yes
2 ☐ No
88 ☐ Don't know
99 ☐ Refused

30. Have you been near or handled a bird nest in the past three weeks? **[30.BirdNest]**

1 ☐ Yes
2 ☐ No
88 ☐ Don't know
99 ☐ Refused

31. How many large trees overhang your property? **[31.NumTrees]**

1 ☐ None
2 ☐ 1-4
3 ☐ 5 or more
88 ☐ Don't know
99 ☐ Refused

What pets do you have?

32. Dog(s) **[32.Dogs]**

1 ☐ Yes (number _____) **[32a.DogsNum]**
2 ☐ No

33. Cat(s) **[33.Cats]**

1 ☐ Yes (number _____) **[33a.CatsNum]**
2 ☐ No

34.Bird(s) **[34.Birds]**

1 ☐ Yes (number _____) **[34a.BirdsNum]**
2 ☐ No

35. Other **[35.OtherPet]**

1 ☐ Yes (Specify_____ number _____)
(Specify_____ number _____)
(Specify_____ number _____)
2 ☐ No

CASE CONTROL STUDY OF LEGIONNAIRES' DISEASE **Study ID:**

CONTROL QUESTIONNAIRE

Gardening Behaviour

Soil

Now we will go through a series of questions about how you use and handle soil. Later I will ask the same questions specifically in relation to potting mix and compost.

(interviewer may refer to definitions of soil, potting mix, and compost if necessary)

36. In the past three weeks, have you handled or worked with soil? **[36.Soil3Wks]**

1 ☐ Yes ➔ Go to 37

2 ☐ No ➔ **Go to 46 (*Compost*, page 10)**

88 ☐ Don't know ➔ Go to 46 (page 10)

99 ☐ Refused ➔ Go to 46 (page 10)

37. Please describe how you used and handled soil the last time you used it.
(Interviewer to prompt participant and tick responses that arise)

☐ Handled soil in a confined space **[37a.SoilConfSpc] YES=1**

☐ Handled soil in open air **[37b.SoilOpnAir]**

☐ Used soil in outdoor garden **[37c.SoilGardOut]**

☐ Used soil in indoor garden, hot house, tunnel house or conservatory **[37d.SoilGardIn]**

☐ Wetted down soil before use **[37e.SoilWet]**

☐ Tipped soil into a wheelbarrow or garden **[37f.SoilTip]**

☐ Trowelled soil into a wheelbarrow or garden **[37g.SoilTrowel]**

☐ Digging over garden **[37h.DigOverGard]**

☐ Weeding **[37i.Weeding]**

☐ Planting **[37j.Planting]**

☐ Other_____ **[37k.SoilFreeTxt]**

38. The last time you used soil, did you wear gloves? **[38.SoilGloves]**

1 ☐ Yes ➔ Go to 39

2 ☐ No ➔ Go to 40

88 ☐ Don't know

99 ☐ Refused

39. Did your gloves keep you hands entirely clean? **[39.SoilGlvsHnds]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

40. The last time you used soil, did you wear a mask? **[40.SoilMask]**

1 ☐ Yes ➔ Go to 41

2 ☐ No ➔ Go to 43

88 ☐ Don't know ➔ Go to 43

99 ☐ Refused ➔ Go to 43

41. What type of mask did you use? **[41.SoilMaskTyp]**

(Interviewer to prompt participant and tick themes that arise)

1 ☐ Surgical mask with ties

2 ☐ Surgical mask with ear loops

3 ☐ N95 green moulded mask

4 ☐ White moulded dust mask

5 ☐ Other, specify_____ **[41a.SoilMaskSpec]**

42. How did you use the mask?

(Interviewer to prompt participant and tick themes that arise)

☐ Put mask on before handling soil **[42a.SoilMskBefore] YES=1**

☐ Put mask while handling soil **[42b.SoilMskDuring]**

☐ Used a new mask **[42c.SoilMskNew]**

☐ Re-used mask **[42d.SoilMskReused]**

☐ Washed hands after handling soil before removing mask. **[42e.SoilMskWash]**

43. In the past three weeks, have you touched your face during or after using soil before washing your hands? **[43.SoilTchFce]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

44. In the past three weeks, have you eaten food or had a drink during or after using soil before washing your hands? **[44.SoilEatDrink]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

45. In the past three weeks, have you smoked during or after using soil before washing your hands? **[45.SoilSmoke]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

Compost

46. In the past three weeks, have you handled or worked with compost? **[46.Comp3Wks]**

1 ☐ Yes ➔ Go to 47

2 ☐ No ➔ **Go to 61** ***(Potting Mix,* page 13*)***

88 ☐ Don't know ➔ Go to 61 (page 13)

99 ☐ Refused ➔ Go to 61 (page 13)

47. Was the compost purchased or homemade? **[47.CompPurch]**

1 ☐ Purchased

2 ☐ Homemade ➔ Go to 48

3 ☐ Both ➔ Go to 48

88 ☐ Don't know

99 ☐ Refused

48. Do you make compost on site? **[48.CompOnsite]**

1 ☐ Yes ➔ Go to 49

2 ☐ No ➔ Go to 52

88 ☐ Don't know

99 ☐ Refused

49. Is the compost made/stored in an open or closed container? **[49.CompBinTyp]**

1 ☐ Open bin

2 ☐ Closed container

3 ☐ Both

88 ☐ Don't know

99 ☐ Refused

50. Have you turned or stirred your homemade compost in the past three weeks? **[50.CompStir]**

1 ☐ Yes ➔ Go to 51

2 ☐ No ➔ Go to 52

88 ☐ Don't know

99 ☐ Refused

51. How long had it been since you previously stirred or turned your compost? **[51.CompStrPrv]**

_____ weeks

52. Please describe how you used and handled compost the last time you used it. (Interviewer to prompt participant and tick responses that arise)

☐ Opened or accessed compost in a confined space **[52a.CompConfSpce] YES=1**

☐ Opened or accessed compost in open air **[52b.CompOpnAir]**

☐ Cut opened compost bag **[52c.CompCutBag]**

☐ Ripped open compost bag **[52d.CompRipBag]**

☐ Used compost in outdoor garden **[52e.CompOut]**

☐ Used compost in indoor garden, hot house, tunnel house or conservatory **[52f.CompIn]**

☐ Wetted down compost before use **[52g.CompWet]**

☐ Tipped compost into a wheelbarrow or garden **[52h.CompTip]**

☐ Trowelled compost into a wheelbarrow or garden **[52i.CompTrowel]**

☐ Moved or transferred compost with hands **[52j.CompHands]**

☐ Other_____ **[52l.CompFreeTxt]**

53. The last time you used compost, did you wear gloves? **[53.CompGlvs]**

1 ☐ Yes ➔ Go to 54

2 ☐ No ➔ Go to 55

88 ☐ Don't know ➔ Go to 55

99 ☐ Refused ➔ Go to 55

54. Did your gloves keep you hands entirely clean? **[54.CompGlvsCln]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

55. The last time you used compost, did you wear a mask? **[55.CompMsk]**

1 ☐ Yes ➔ Go to 56

2 ☐ No ➔ Go to 58

88 ☐ Don't know

99 ☐ Refused

56. What type of mask did you use? **[56.CompMskTyp]**

(Interviewer to prompt participant and tick themes that arise)

1 ☐ Surgical mask with ties

2 ☐ Surgical mask with ear loops

3 ☐ N95 green moulded mask

4 ☐ White moulded dust mask

5 ☐ Other, specify_____ **[56.CompMskSpec]**

57. How did you use the mask?

(Interviewer to prompt participant and tick themes that arise)

☐ Put mask on before handling compost **[57a.CompMskBefore] YES=1**

☐ Put mask while handling compost **[57b.CompMskDuring]**

☐ Used a new mask **[57c.CompMskNew]**

☐ Re-used mask **[57d.CompMskUsed]**

☐ Washed hands after handling compost before removing mask **[57e.CompMskWsh]**

58. In the past three weeks, have you touched your face during or after using compost before washing your hands? **[58.CompFace]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

59. In the past three weeks, have you eaten food or had a drink after using compost before washing your hands? **[59.CompEatDrink]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

60. In the past three weeks, have you smoked after using compost before washing your hands? **[60.CompSmoke]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

Potting Mix

61. In the past three weeks, have you handled or worked with potting mix? **[61.PtgMx3Wks]**

1 ☐ Yes ➔ Go to 62

2 ☐ No ➔ **Go to 73 (Health Questions, page 16)**

88 ☐ Don't know ➔ Go to 73, page 16

99 ☐ Refused ➔ Go to 73, page 16

62. Was the potting mix purchased or homemade? **[62.PtgMxPurch]**

1 ☐ Purchased

2 ☐ Homemade

3 ☐ Both

88 ☐ Don't know

99 ☐ Refused

63. Please describe how you used and handled potting mix the last time you used it. (Interviewer to prompt participant and tick responses that arise)

☐ Opened potting mix in a confined space **[63a.PtgMxConfSpc] YES=1**

☐ Opened potting mix in open air **[63b.PtgMxOpnAir]**

☐ Cut open potting mix bag **[63c.PtgMxCut]**

☐ Ripped open potting mix bag **[63d.PtgMxRip]**

☐ Used potting mix in outdoor garden **[63e.PtgMxOut]**

☐ Used potting mix in indoor garden, glasshouse/tunnel house,conservatory **[63f.PtgMxIn]**

☐ Wetted down potting mix before use **[63g.PtgMxWet]**

☐ Tipped potting mix into a wheel barrow or garden **[63h.PtgMxTip]**

☐ Trowelled potting mix into a wheel barrow or garden **[63i.PtgMxTrowel]**

☐ Moved or transferred potting mix with hands **[63j.PtgMxHands]**

☐ Other_____ **[63k.PtgMxOther]**

64. The last time you used potting mix, did you wear gloves? **[64.PtgMxGloves]**

1 ☐ Yes ➔ Go to 65

2 ☐ No ➔ Go to 66

88 ☐ Don't know

99 ☐ Refused

65. Did your gloves keep you hands entirely clean? **[65.PtgMxClean]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

66. The last time you used potting mix, did you wear a mask? **[66.PtgMxMask]**

1 ☐ Yes ➔ Go to 67

2 ☐ No ➔ Go to 69

88 ☐ Don't know

99 ☐ Refused

67. What type of mask did you use? **[67.PtgMxMskTyp]**
(Interviewer to prompt participant and tick responses that arise)

1 ☐ Surgical mask with ties

2 ☐ Surgical mask with ear loops

3 ☐ N95 green moulded mask

4 ☐ White moulded dust mask

5 ☐ Other, specify_____

68. How did you use the mask?
(Interviewer to prompt participant and tick responses that arise)

☐ Put mask on before handling potting mix **[68a.PtgMxMskBefore] YES=1**

☐ Put mask while handling potting mix **[68b.PtgMxMskDuring]**

☐ Used a new mask **[68c.PtgMxMskNew]**

☐ Re-used mask **[68d.PtgMxMskUsed]**

☐ Washed hands after handling potting mix before removing mask. **[68e.PtgMxMskWash]**

CONTROL QUESTIONNAIRE

69. In the past three weeks, have you touched your face during or after using potting mix before washing your hands? **[69.PtgMxFace]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

70. In the past three weeks, have you eaten food or had a drink after using potting mix (with or without gloves) before washing your hands? **[70.PtgMxEatDrnk]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

71. In the past three weeks, have you smoked after using potting mix (with or without gloves) before washing your hands? **[71.PtgMxSmoke]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

72. Are you aware of health risks relating to potting mix? **[72.PtgMxRisks]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

HEALTH QUESTIONS

Tobacco Use

73. Have you ever smoked a total of more than *100* cigarettes in your whole life? **[73.100Cig]**

1 ☐ Yes ➔ Go to 74

2 ☐ No ➔ **Go to 80 (*Alcohol,* page 17*)***

88 ☐ Don't know ➔ Go to 80

99 ☐ Refused ➔ Go to 80

74. How old were you when you started smoking regularly? [Record in years] **[74.AgeSmk]**

_____

88 ☐ Don't know **[74a.AgeSmkDN/R]**

99 ☐ Refused

75. How often do you now smoke? **[75.FreqSmk]**

(Read answer options. If more than one frequency given, tick the highest one)

1 ☐ You don't smoke now

2 ☐ Less often than once a month

3 ☐ At least once a month

4 ☐ At least once a week

5 ☐ At least once a day

88 ☐ Don't know

99 ☐ Refused

76. How old were you when you stopped smoking regularly (daily)? [Record in years] **[76.AgeStopSmk]**

_____

88 ☐ Don't know **[76a.AgeStopSmk]**

99 ☐ Refused

77. From when you started smoking regularly to now/when you stopped, did you ever give up smoking for 6 months or more? **[77.StopSmk6Mnths]**

1 ☐ Yes, once

2 ☐ Yes, twice

3 ☐ Yes, three times or more

4 ☐ No ➔ Go to 79

88 ☐ Don't know ➔ Go to 79

99 ☐ Refused ➔ Go to 79

78. In total, taking into consideration all the times you stopped, how long did you give up smoking for? [Record in years] **[78.StopSmkYrs]**
(Round to the nearest year)

_____

88 ☐ Don't know **[78.StopSmkYrsDN/R]**

99 ☐ Refused

CONTROL QUESTIONNAIRE

79. On average, over all your years of smoking, how many cigarettes do/did you smoke a day? **[79. AveCigsDay]**

(If respondent is unable to suggest an average, ask for the typical number of cigarettes smoked in a week and divide by 7)

1 ☐ Less than 1 per day
2 ☐ 1-5 per day
3 ☐ 6-10 per day
4 ☐ 11-15 per day
5 ☐ 16-20 per day
6 ☐ 21-25 per day
7 ☐ 26-30 per day
8 ☐ 31 or more a day
88 ☐ Don't know
99 ☐ Refused

Alcohol

80. Have you had a drink containing alcohol in the last year? **[80.AlcYear]**

1 ☐ Yes ➔ Go to 81
2 ☐ No ➔ **Go to 84, *Asthma***
88 ☐ Don't know ➔ Go to 84
99 ☐ Refused ➔ Go to 84

81. How often do you have a drink containing alcohol? **[81.AlcFreq]**

1 ☐ Monthly or less
2 ☐ Up to 4 times a month
3 ☐ Up to 3 times a week
4 ☐ 4 or more times a week
88 ☐ Don't know
99 ☐ Refused

82. How many drinks containing alcohol do you have on a typical day when you are drinking? **[82.NumDrinks]**
(Take average and round to nearest whole number if necessary e.g. if respondent says 4 or 5, average is 4.5, round to nearest whole number = 5, that is code 3)

1 ☐ 1 or 2
2 ☐ 3 or 4
3 ☐ 5 or 6
4 ☐ 7 to 9

5 ☐ 10 or more
88 ☐ Don't know
99 ☐ Refused

83. How often do you have six or more drinks on one occasion? **[83.Freq6Drinks]**

1 ☐ Never
2 ☐ Less than monthly
3 ☐ Monthly
4 ☐ Weekly
5 ☐ Daily or almost daily
88 ☐ Don't know
99 ☐ Refused

Health Conditions

Asthma

84. Have you ever been told by a doctor that you have asthma? **[84.Asthma]**

1 ☐ Yes ➔ Go to 85
2 ☐ No ➔ Go to 86
88 ☐ Don't know
99 ☐ Refused

85. In the last 12 months, how many asthma attacks have you had? **[85.AsthmaAttk]**

1 ☐ None
2 ☐ 1-5
3 ☐ 6-10
4 ☐ 11-15
5 ☐ More than 15
88 ☐ Don't know
99 ☐ Refused

COPD (Chronic obstructive pulmonary disease)

86. Have you ever been told by a doctor that you have chronic bronchitis or emphysema? **[86.COPD]**

1 ☐ Yes
2 ☐ No
88 ☐ Don't know

99 ☐ Refused

Heart disease

87. Have you ever been told by a doctor that you have had a heart attack, have angina (typically chest pain when you walk or do exercise), or other heart disease? **[87.HeartDis]**

1 ☐ Yes, specify if other _____ **[87a.HeartDisSpec]**

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

Diabetes

88. Have you ever been told by a doctor that you have diabetes? **[88.Diabetes]**

1 ☐ Yes

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

Other health conditions

89. Do you have any other on-going or regularly occurring medical conditions? **[89.OthrMedCond]**

1 ☐ Yes, Specify: _____ **[89.OthrMedCondSpec]**

2 ☐ No

88 ☐ Don't know

99 ☐ Refused

CASE CONTROL STUDY OF LEGIONNAIRES' DISEASE **Study ID:**

CONTROL QUESTIONNAIRE

Current Medication

90. What are your current medications/prescriptions for yourself? Please include all medications such as inhalers, aerosol, injections, tablets and 'over the counter medication' etc. **[Medication-Table 2]**

Please read from the packet or bottle if possible and tell me the drug name, dose and number taken per day.

Drug Name – Prescription drugs from a Doctor	Dose	Number/day

Participant Details

91. What is your date of birth? _____/_____/_____ **[91.DateOfBirth]**

92. Are you male or female? **[92.Gender]**

1 ☐ Male

2 ☐ Female

93. What ethnic group or groups do you belong to? **[93.Ethnicity]**

1 ☐ New Zealand European

2 ☐ Māori

3 ☐ Samoan

4 ☐ Cook Island Māori

5 ☐ Tongan

6 ☐ Niuean

7 ☐ Chinese

8 ☐ Indian

9 ☐ Other, such as Dutch, Japanese, Tokelaua, specify_____**[93.EthnicitySpec]**

88 ☐ Don't know

94. What is your current occupation? **[94.Occupation]**
Specify_____

95. What is the total income that *you yourself* got from *all sources*, before tax or anything was taken out of it, in the last 12 months? **[95.Income]**

1 ☐ Less than $15,000
2 ☐ $15,001 - $40,000
3 ☐ $40,001 - $70,000
4 ☐ $70,001 - $100,000
5 ☐ $100,001 - $150,000
6 ☐ $150,001 +
88 ☐ Don't know
99 ☐ Refused

96. What is the total income that *everyone in your household* got from *all sources*, before tax or anything was taken out of it, in the last 12 months? **[96.HsehldIncome]**

1 ☐ Less than $15,000
2 ☐ $15,001 - $40,000
3 ☐ $40,001 - $70,000
4 ☐ $70,001 - $100,000
5 ☐ $100,001 - $150,000
6 ☐ $150,001 +
88 ☐ Don't know
99 ☐ Refused

Thank you very much for providing this information… just two final questions.

97. Are you interesting in receiving the results of the study? **[97.StudyResults]**

1 ☐ Yes
2 ☐ No

98. Would it be ok if we contacted you again if we need any further information about your responses? **[98.FollowUp]**

1 ☐ Yes
2 ☐ No